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ABSTRACTS OF WORLD MEDICINE

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ABSTRACTS OF WORLD MEDICINE

This journal is planned to provide the reader with a selection of abstracts of the more important articles appearing in medical periodicals published in different parts of the world. Comment by the abstracter, when thought necessary, is inserted between square brackets, usually at the end of an abstract. In some instances only the titles of articles are provided.

The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals* and in *World Medical Periodicals*. The titles of articles from foreign journals are translated into English.

This journal is essentially a guide to work in progress in the world's medical centres. No abstract can be regarded as a substitute for the article abstracted. For complete information the original article must be consulted. Our aim is to give the reader sufficient details in an abstract to enable him to judge whether the original is, for him, worth reading in full.

The abstracts are grouped in broad classifications and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together under the same heading. The specialist will, it is hoped, learn from this journal of work done in other fields as well as in his own. The general practitioner will be able to keep abreast of modern knowledge in the various specialties. The representation in one journal of the several aspects of Medicine will, it is believed, give an integrated picture of the whole, necessary in this age of specialization.

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ABSTRACTS OF WORLD MEDICINE

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Pathology

EXPERIMENTAL PATHOLOGY

892. **Effect of Hyaluronidase on Inflammation**
J. M. GLASSMAN, A. BLUMENTHAL, W. J. BECKFIELD, and J. SEIFTER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **82**, 323–328, Feb., 1953. 2 figs., 7 refs.

The effect of hyaluronidase on the local inflammation caused by two irritating drugs, allyl *iso*thiocyanate and *para*phenylenediamine, was investigated at the University of Pennsylvania.

The drugs were injected intradermally into 46 albino rabbits; after one minute 0·1 ml. of hyaluronidase (containing 900 turbidity-reducing units) was introduced into some of the injection sites and 0·1 ml. of saline solution into the other sites. After 15 minutes trypan blue, 10 mg. per kg. body weight, was given intravenously to each rabbit. The area of spread of the dye was measured at varying intervals thereafter, the injection sites being finally examined microscopically.

It was found that when the irritants were given with hyaluronidase the area of spread was greater than when no hyaluronidase was given; the enzyme, however, appeared to be responsible for an absence of swelling. Microscopically, there was very much less oedema but a greater degree of extravasation of erythrocytes with hyaluronidase, other inflammatory features being apparently unaffected.

It is suggested that increased filtration through the capillary wall leads locally to a lowering of the concentration of the irritant and to an accelerated diffusion of the oedema fluid away from the site of injury.

G. Loewi

893. **A Contribution to the Problem of the Influence of the Higher Nervous Functions on the Development of Experimental Tumours.** (К вопросу о влиянии высшей нервной деятельности на развитие экспериментальных опухолей)
E. P. KOJEVNIKOVA. *Архив Патологии* [*Arkh. Patol.*] 15, 22–27, 1953. 4 figs., 4 refs.

An investigation is described into the influence of disturbances of cortical function on the development of tumours induced by methylcholanthrene in the skin of mice. Local applications of a 0·5% solution of methylcholanthrene in benzene were made to the skin of the interscapular region of all animals. The control group were not subjected to any other experimental procedure, but in the animals in the test group two conditioned reflexes had been developed, one protective, in response to the sound of an electric bell followed by an electric shock, the other in response to a whistle followed by feeding. A " nervous breakdown " was then produced by simultaneous sounding of the electric bell and the whistle. The mice are described as having become "neurotic".

A comparison of the incidence of induced tumours in the test and control groups of animals during the 7th month of an experiment on a total of 82 animals showed a striking difference, namely, 54·1% in the test group as against 20·7% among the controls. In a second series of 84 mice (43 test animals and 41 controls) in which a " neurosis " had been induced by a somewhat more complicated mechanism of two conditioned reflexes, the conditioning stimuli of which were subsequently reversed, the incidence of tumours after 3 months was 43·3% in the test group and only 16·6% among the controls.

The author concludes that a normal balanced activity of the central nervous system plays some part in the protection of the organism against the development of malignant tumours.

A. Swan

894. **Agar Culture of Exudates**
R. J. V. PULVERTAFT and W. H. W. JAYNE. *Annals of the Royal College of Surgeons of England* (*Ann. roy. Coll. Surg. Engl.*) **12**, 161–173, March, 1953. 20 figs., 4 refs.

A simple method is described by which cells from malignant or benign exudates or in scrapings from tumours of animals or man may be kept alive for several days, and their appearance and behaviour observed. A medium consisting of equal parts of diluted ascitic or pleural exudate and Tyrode's solution with 0·75% of agar and 10 units of penicillin per ml. is cast in small Petri dishes; when set, small blocks are cut out and transferred to slides. A drop of cell suspension is placed on the block of medium, and a coverslip supported on soft wax pillars is pressed down over it until fluid contact is made. Exudate should be treated with an anticoagulant such as heparin or sodium citrate and must be examined within the shortest possible time of collection. The preparation is observed by phase-contrast microscopy, and is suitable for cinematographic recording

The characteristics of polymorphonuclear leucocytes lymphocytes, endothelial cells, and tumour cells are

described. No claim is made that malignancy can be reliably diagnosed, but certain features, for example, the translucency of the nucleus and a tendency to form three-dimensional groups, are characteristic of tumour cells.

Cells are said to remain alive for at least 5 days [but some of the criteria of viability adopted are open to question]. Occasionally mitoses, especially among the lymphocytes, were seen after as long as a week.

M. H. Salaman

895. **Erythrophagocytosis: Standardization of a Quantitative Tissue Culture Test and Its Application to Hemolytic, Malignant, and Infectious Diseases**

C.-S. WRIGHT, M. C. DODD, N. G. BRANDT, S. M. ELLIOTT, and J. A. BASS. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **41**, 169–178, Feb., 1953. 3 figs., 21 refs.

The authors have found that the usual laboratory procedures carried out *in vitro* for determination of the factors influencing normal and abnormal destruction of erythrocytes provide a very inadequate index of the changes which actually occur *in vivo*. With particular reference to the role played by phagocytosis they have devised a test at Ohio State University to investigate the susceptibility of human erythrocytes to phagocytosis by rabbit splenic macrophages. The procedure is fully described. Essentially, it consists in the culture of a small fragment of rabbit's spleen on the coverslip of a slide cell, to which washed erythrocytes from a human subject are then added. After incubation for 30 minutes at 37° C., 50 macrophages in each culture are inspected and the number containing erythrocytes noted, the percentage of macrophages showing phagocytosis being taken as the standard " phagocytic index ".

It was found that in 59 apparently healthy subjects the phagocytic index ranged from 0 to 12, with a median value of 3. The test was then applied to 293 patients divided into 3 groups suffering from (1) haemolytic anaemia, (2) malignant disease, (3) infectious diseases. The median phagocytic index in Group 1 was 34 ; in Group 2 the index ranged from 18 to 48 ; and in Group 3 the median value was 25, high values being obtained in tuberculosis (up to 88) and hepatitis (54).

It is concluded that the condition of the erythrocytes plays the paramount role in determining the amount of phagocytosis, that in disease certain factors which modify the erythrocytes are at work, and that this test is of value in detecting these changes. The nature of only some of these modifying factors is at present known, but further study is in progress.

D. M. Pryce

896. **A Specific Inhibitor for Human Desoxyribonuclease and an Inhibitor of the Lupus Erythematosus Cell Phenomenon from Leucocytes**

N. B. KURNICK, L. I. SCHWARTZ, S. PARISER, and S. L. LEE. *Journal of Clinical Investigation* [*J. clin. Invest.*] **32**, 193–201, March, 1953. 6 figs., 27 refs.

In experiments performed at Tulane University School of Medicine, New Orleans, extracts of leucocytes which had been disintegrated by freezing and thawing were shown to contain an inhibitor for human desoxyribose nuclease. The authors investigated the chemical nature of this factor and found it to be a relatively stable protein. Its properties were very similar to those of the inhibitor of the " L.E.-cell " phenomenon previously demonstrated in leucocytes, and the authors suggest that these two inhibitors are identical.

Marjorie Le Vay

897. **The Effect of Corticotropin (ACTH), Dihydrostreptomycin, and Corticotropin–Dihydrostreptomycin on Experimental Bovine Tuberculosis in the Rabbit**

J. M. BACOS and D. T. SMITH. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 201–211, Feb., 1952. 7 figs., 25 refs.

A series of controlled experiments was carried out at Duke University School of Medicine, Durham, North Carolina, to ascertain the effect of administration of corticotrophin, dihydrostreptomycin, and a combination of these two drugs on the course of pulmonary tuberculosis in previously sensitized, partially immune rabbits. It was found that corticotrophin did not greatly reduce the resistance of animals previously sensitized to tuberculosis, and that the drug could be administered with safety if dihydrostreptomycin was given simultaneously.

Kenneth Marsh

898. **Experimental Production of Arthritis in Rats by Hypophyseal Growth Hormone**

W. O. REINHARDT and CHOH HAO LI. *Science* [*Science*] **117**, 295–297, March 20, 1953. 2 figs., 6 refs.

The experiments described in this paper from the University of California were undertaken to determine the role, if any, of the pituitary growth hormone in the production of chronic arthritis in the absence of the adrenal glands and gonads. Of 38 plateaued [*sic*] female rats, 6 to 8 months old, 18 were subjected to adrenalectomy and ovariectomy, the remainder serving as controls. Gradually increasing daily doses of pituitary growth hormone were given by intraperitoneal injection to 10 rats in each group for a period of 6 months. All the animals were maintained on saline and a stock diet in comparable environmental conditions. At the end of the 6-month period the weight of the animals receiving growth hormone in both groups was 65% greater than that of untreated normal controls, but the former became sluggish and irritable. Knee- and ankle-joints became tender, and there were transient episodes of joint swelling.

Radiographs of all treated animals disclosed joint disturbances, especially at the knee, characterized by irregularities and erosions of the condylar margins, local osteoporotic areas, and lipping and calcification at the joint margins. During the experiments 2 of the animals, which were in poor condition, were given hydrocortisone for one week, with apparent improvement.

The significance of these results is briefly discussed. It is pointed out, however, that the evidence provided by the experiments " does not preclude the possible existence of sensitization to growth hormone or of production of hypersensitivity to other allergenic factors ".

C. L. Cope

899. **Experimental Studies of the " Endocrine Kidney " of Selye.** (Experimentelle Untersuchungen zur " Endokrinen Niere " (Selye))

A. BOHLE, M. KOHLER, and H. BUROW. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* [*Virchows Arch. path. Anat.*] **323**, 1–23, 1953. 9 figs., 45 refs.

In experiments carried out at the University of Heidelberg on 148 rats, 130 to 170 g. in weight, the aorta was partly occluded by means of a clamp between the origins of the two renal arteries so that the blood supply to the more distal was reduced. In 19 animals this resulted in the development of an " endocrine kidney " as defined by Selye, in 30 the kidney showed only an incomplete collapse of the tubules or circumscribed necrotic patches, and in the remaining 99 animals the kidney either became completely necrotic or remained normal. The period of observation was 2 to 4 weeks (in contrast to Selye's 14 days).

In the animals in which the " endocrine kidney " developed there was transient rise of blood pressure (up to 165 mm. Hg), as in the case of a unilateral " Goldblatt kidney ", but contrary to Selye's findings persistent hypertension was not observed. Moreover, although the epithelioid cells of the afferent arterioles were increased in number in the kidneys of these animals, no epithelial proliferation was found in the distal convoluted tubules. Hence Selye's hypothesis that renin is produced in the latter is rejected by the present authors, who incline towards Goormaghtigh's view that the epitheloid cells of the afferent arterioles are responsible for the formation of renin, although this could not be demonstrated. In their opinion the term " endocrine kidney " is misleading, and should be replaced by " collapse kidney ", the condition being the result of passive collapse of the renal tubules. *V. C. Medvei*

CHEMICAL PATHOLOGY

900. **Technique and Experiences with Tubeless Gastric Analysis**

S. P. BRALOW, W. SACKS, and M. LIEBERSON. *Journal of the Albert Einstein Medical Center* [*J. Albert Einstein med. Cent.*] **1**, 61–71, Feb., 1953. 12 refs.

In this paper from the Albert Einstein Medical Center, Philadelphia, the authors attempt to evaluate the tubeless gastric-analysis technique proposed by Segal (*Med. Clin. N. Amer.*, 1951, **35**, 593). This method entails the use of a quininium indicator combined with a cation-exchange resin, the substance so formed exchanging quinine ions for hydrogen ions in the presence of free hydrochloric acid in the gastric juice. The free quinine is then absorbed in the gastro-intestinal tract and can be determined easily in blood or urine. Segal emphasizes that this method can reveal only the presence or absence of free gastric acidity, and not the *p*H or total hydrogen-ion content of the gastric juice. He limits the use of this resin compound to the screening of patients for achlorhydria.

The present authors confirm Segal's observation that this method provides a reliable means of detecting achlorhydric patients. According to them, the indicator-resin technique can also be used to detect hyperchlorhydria, but the excretion level indicating hypersecretion has to be determined for each batch of resin. They find that the method has the drawback that the indicator is not liberated from the resin stoichiometrically by hydrogen cations. It appears, however, to reflect gastric hyperchlorhydria as well as achlorhydria, provided there is no renal or hepatic dysfunction. As 60 to 70% of the quinine is normally destroyed by the liver, high levels of excretion may reflect abnormal liver function rather than hyperchlorhydria. Normally one-third of the absorbed quinine is excreted in the urine within 3 hours; this excretion may be delayed in cases of kidney disease, leading to a false diagnosis of achlorhydria.

It is also pointed out that although tubeless gastric analysis is less unpleasant than intubation and may give information as to hypersecretion and achlorhydria, it gives no information as to gastric retention, motility, or digestive ability. *E. Forrai*

901. **Urinary Excretion of the Pressor Amines in Relation to Phaeochromocytoma**

G. P. BURN. *British Medical Journal* [*Brit. med. J.*] **1**, 697–699, March 28, 1953. 13 refs.

In some cases patients with hypertension appear to owe their symptoms to the release of adrenaline, or more usually to the non-methylated substance noradrenaline, from an adrenal gland in which the medullary tissue is greatly hypertrophied. In this study, reported from the Radcliffe Infirmary and the University Department of Biochemistry, Oxford, the urinary output of pressor substances, extracted by Euler's method and estimated biologically as though all in the form of noradrenaline, was determined in 38 normotensive subjects ranging in age from 3 months to 63 years, in 15 middle-aged subjects with a raised blood pressure (over 130 mm. Hg systolic), in 6 cases of toxaemia of pregnancy and 7 of normal pregnancy, and in 3 patients with phaeochromocytoma causing paroxysmal hypertension.

No difference in the amount of pressor amines excreted was found between the subjects with normal and those with raised blood pressure, or between women in normal pregnancy and those with toxaemia of pregnancy. The urinary excretion of pressor amines in the 3 cases of phaeochromocytoma, from each of which an adrenal tumour was removed at subsequent operation, showed a wide variation, and the lowest figure obtained was not much higher than the highest figure in normal subjects. It is considered that the value of the determination of pressor amines in the urine seems to be confined to the diagnosis of phaeochromocytoma, and even in these cases it is important to make the urinary estimations during a period in which paroxysms of hypertension are occurring. *L. A. Elson*

902. **A Modified Method for Estimating 17-Hydroxycorticosteroids in Plasma**

R. I. S. BAYLISS and A. W. STEINBECK. *Biochemical Journal* [*Biochem. J.*] **54**, 523–527, 1953. 18 refs.

HAEMATOLOGY

903. Clinical Value of Eosinophil Counts and Eosinophil Response Tests

W. R. Best, R. M. Kark, R. C. Muehrcke, and M. Samter. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 702–706, Feb. 28, 1953.

The revival of interest in the eosinophilic granulocyte, that " beautiful but mysterious cell ", has been due to two recent discoveries, that adrenal cortical activity produces eosinopenia, and that the absolute eosinophil count is fairly simply performed and much more accurate than the differential count.

At the University of Illinois College of Medicine eosinophil counts were made using Randolph's stain (0·1% phloxine in equal parts of propylene glycol and distilled water) and taking the average of 4 chambers. The limits of normal (at 8 a.m. in 42 healthy men) were 70 and 450 cells per c.mm. There was a mid-morning fall in the count by about 20%, and an evening rise to about 30% above the normal 8-a.m. count.

The commonest cause of a rise in the eosinophil count is an antigen–antibody reaction of the anaphylactic type. The authors discuss and give a full list of the causes of eosinophilia and eosinopenia. In the diagnosis of Addison's disease it was shown that if the Thorn test is carried out by giving intravenously over 4 hours 50 units of ACTH in 500 ml. of 5% glucose, there will be a profound fall in the eosinophil count after a further 4 hours in those with intact adrenals, and poor response in cases of Addison's disease. The adrenaline-response test was not found to be reliable. Eosinophil counts are useful in ACTH therapy but not necessary during treatment with cortisone. *G. S. Crockett*

904. A Study of the Erythrocyte Sedimentation Rate for Well Children

N. F. Hollinger and S. J. Robinson. *Journal of Pediatrics* [*J. Pediat.*] **42**, 304–319, March, 1953. 2 figs., bibliography.

Although the erythrocyte sedimentation rate is widely accepted as a diagnostic aid, its normal variation and accuracy, and even its clinical significance, the authors declare, have never been clearly established, particularly in regard to children. In an attempt to remedy this defect the erythrocyte sedimentation rate (E.S.R.) of 293 children aged from 4 to 15 years and judged to be clinically well was determined at the School of Public Health (University of California), Berkeley, by three established techniques, namely, the Wintrobe method, the Westergren method modified by the use of Wintrobe's anticoagulant mixture instead of citrate, and by the micromethod of Landau and Adams, also modified by the use of blood collected into Wintrobe's dry anticoagulant before diluting with sodium citrate solution in the bulb.

From their own results and a survey of the literature the authors draw a number of conclusions. The E.S.R. for healthy children aged 4 to 15 years ranged from 0 to 20 mm. in 1 hour both by the uncorrected Wintrobe and the Landau–Adams techniques, although about 5 to 10% of apparently well children may have a rate higher than 20 mm. The younger children, aged 4 to 11 years, had a higher rate (average 12 mm.) than children aged 12 to 15 years (average 7·5 mm.). The authors found that the correlation between the three methods when applied to the same specimen of blood was very high, and they consider that employment of any of these methods would give similar results. The type of anticoagulant used made little difference to the result. However, when 30 estimations were made on one sample of blood, readings at 1 hour were found to vary by ± 5 mm. with Wintrobe's method, ± 7 mm. with the Landau–Adams microtechnique, and by ± 4 mm. with Westergren's method. This variation must therefore be borne in mind when considering the clinical significance of the result when determined by a single technique. They believe that in children correction for anaemia is not necessary, since the correlation between the corrected and uncorrected E.S.R. by the Wintrobe method is extremely high (0·95). The packed cell volume was also determined and was found to increase gradually with the year of age, the average being 40% in the age group 4–11, and 43% in the age group 12–15. *R. F. Jennison*

MORBID ANATOMY AND CYTOLOGY

905. Bronchogenic Cysts: a Manifestation of Congenital Polycystic Disease of the Lungs

E. L. Heller, J. H. Householder, and A. M. Benshoff. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **23**, 121–128, Feb., 1953. 5 figs., 17 refs.

The authors describe, from the Presbyterian and the Woman's Hospitals, Pittsburgh, Pennsylvania, 7 cases of bronchogenic cyst. Their clinical and radiological features are enumerated and the differential diagnosis is discussed. Though the radiological appearances in all 7 cases were those of a solitary cyst, in 3 of them an opportunity was presented of examining a whole lobe or lung, and in 2 of these microscopical examination disclosed associated small cysts similar in structure to the large cyst. It is therefore suggested that the bronchogenic cyst is an incompletely developed manifestation of congenital polycystic disease in the lung and of identical pathogenesis. *J. B. Wilson*

906. Primary Alveolar Cell Carcinoma of the Lung

J. H. Fisher and W. J. Holley. *Archives of Pathology* [*Arch. Path. (Chicago)*] **55**, 162–170, Feb., 1953. 6 figs., 10 refs.

The authors describe very briefly 6 cases of so-called primary alveolar-cell carcinoma of the lung, in 5 of which the diagnosis was proved at necropsy and in one by biopsy of a lymph node, and in all of which there were widespread small, even miliary, tumour masses throughout both lungs. The histological picture of the pulmonary masses and of the secondary growths was that of an adenocarcinoma of low-grade malignancy which, in the lungs, consisted of columnar or cuboidal cells lining the alveoli, usually forming a single layer and

occasionally forming papillary projections into the alveoli. In one case some of the cells bore cilia, and mucin was present in the cells and alveolar spaces in all cases, occasionally to such an extent as to fill the alveoli. The authors point out that the pulmonary alveoli are mesodermal in origin, whereas the appearance and behaviour of this type of tumour suggest strongly that it is of epithelial nature. They therefore conclude that it arises from bronchial epithelium, probably that of the terminal bronchioles; the fact that they could not demonstrate a primary growth in any of the cases examined at necropsy suggests that it is of multicentric origin. While the characteristics of this tumour are such as to justify a separate classification on histological grounds, nothing pathognomonic could be found in the clinical picture or radiological appearances in the authors' cases.

A. Gordon Signy

907. **Miniature Carcinoma and Microcarcinoma of the Bronchus and their Relation to the " Alveolar-cell Carcinoma " of the Lung.** (Zu den Miniatur- und Mikrokarzinomen der Bronchien und ihren Beziehungen zum " Alveolarzellkarzinom " der Lunge)

W. WERNER. *Zentralblatt für allgemeine Pathologie und pathologische Anatomie* [*Zbl. allg. Path. path. Anat.*] **90**, 1–14, Feb. 26, 1953. 15 figs., bibliography.

The author records, from the St. Georg Municipal Hospital, Leipzig, 5 cases of secondary carcinoma of the lung in which the primary tumour in the bronchus was very small. In one of these the growth was situated at the periphery of the lung near the pleura, producing a scirrhous reaction. Spread had occurred via the lymphatic system as well as directly, producing the features of a carcinomatous pneumonia. Histologically the alveoli were found to be intact, but to be loosely covered by a single row of tall carcinomatous cells. In another of the cases described the primary tumour was situated in the thyroid. Mainly on the basis of these 2 cases the author postulates that alveolar-cell carcinoma of the lung represents metastatic growth, the primary tumour being usually so small as to escape detection. The rarity of this type of carcinoma he explains by the fact that apparently only highly differentiated types of carcinoma are capable of spreading in this fashion. *R. Salm*

908. **Histopathologic Studies of Pigmented Nevi in Children**

O. C. STEGMAIER and H. MONTGOMERY. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **20**, 51–64, Jan., 1953. 5 figs., 20 refs.

Pigmented naevi removed from 98 children aged 1 year to 10 years at Dixon State Hospital, Illinois, were examined histologically for evidence of malignancy. Of the total of 100 naevi, 5 contained no recognizable " naevus cells ", 14 were lentigines (that is, without nests of melanoblast proliferation), 47 were pure junction naevi (with nests of melanoblasts in the line of the dermo-epidermal junction), and 34 were combined naevi (that is, with naevus cells in both the cutis and the epidermis). Transition from lentigines to junction naevi was observed in some instances. The incidence of combined naevi was higher in children aged 5 to 10 years than in the younger age group, a finding which suggests a progressive development. *Lames foliacées* were not observed in any case, and mitoses only rarely, but axons were demonstrated in 14 cases. Naevi from the hands and feet did not differ from those from other sites. In no case in this series was malignant melanoma found.

[The distinguishing features of melanomata in children and adults have already been emphasized, but studies of naevi in children have generally been concerned with lesions in which there was clinical evidence of activity. The present investigation indicates that even the most inactive-looking lesions in children constantly show " junctional " change.] *Bernard Lennox*

909. **Microscopic Differential Diagnosis of Latent Carcinoma of Prostate**

R. S. TOTTEN, M. W. HEINEMANN, P. B. HUDSON, E. E. SPROUL, and A. P. STOUT. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **55**, 131–141, Feb., 1953. 7 figs., 10 refs.

In an attempt to detect carcinoma of the prostate in its earliest stages, biopsy was carried out at the Francis Delafield Hospital, New York, on 131 patients with " some significant abnormality of the gland " on palpation, the majority of whom, however, had minimal urinary symptoms or none at all. The posterior lobe of the prostate was exposed through a perineal incision, and a " generous wedge " of tissue removed. Half the material was fixed in Bouin's fluid and frozen, and sections 7 to 10μ thick were stained with metachrome B and examined immediately; the other half was embedded in paraffin for use if necessary. In the majority of cases, however, examination of the frozen sections enabled an unequivocal positive or negative diagnosis to be made. Three easily recognizable histological patterns of carcinoma are described: a cribriform type, a type showing diffuse infiltration by individual cells, and a distinctive type found in glands of medium size. A fourth type of pattern, which was found in small glands and was by far the most common, was not easy to distinguish from that of benign hyperplasia. The usual criteria for the diagnosis of malignancy were applied—invasion, disorderly growth not caused by atrophy or fibrosis, arrangement of the basal epithelium lying irregularly in relation to the acinar epithelium, and irregularity of the cellular details (especially the presence of large, deeply staining nucleoli). Of the 131 patients examined, 15 had clinically obvious carcinoma with metastasis; of the remaining 116 cases, unequivocal histological evidence of carcinoma was found in 24, and in 4 the findings were equivocal. Of the 24 histologically positive cases, the prostatic enlargement in 13 was considered clinically to be benign.

[Only 9 photomicrographs are reproduced to illustrate the different patterns described, and therefore only very obvious examples are shown. There must have been many border-line cases, photomicrographs of which, together with subsequent clinical and pathological confirmation, would have been more instructive.]

A. Gordon Signy

910. **Poliomyelitis. VIII. Studies on Temperature Regulation**

I. A. BROWN, A. B. BAKER, and S. CORNWELL. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **69**, 332–342, March, 1953. 1 fig., 31 refs.

The problem of the exact location of the heat-regulating centre of the body is an old one. As a contribution to its solution, and on the basis of a study at the University of Minnesota School of Medicine of 115 fatal cases of bulbar poliomyelitis, the authors here present the results of their investigation into the correlation between clinical hyperthermia or hypothermia and the histological lesions in the various nuclear areas of the hypothalamus. The hypothalamus was studied in detail in each case and the nuclei were divided into three groups: (1) the supraoptic, paraventricular, and tuberal nuclei, situated in the anterior hypothalamus at the level of the optic chiasma; (2) the dorsomedial, ventromedial, and lateral nuclei in the middle hypothalamus; and (3) the posterior and mammillary nuclei in the posterior hypothalamus at the level of the mammillary body. Rigid criteria were adopted in detecting cases of true hyperthermia, and of the 115 cases, 12 conformed to these criteria.

In all 12 cases severe cell damage, of which the diagnosis was also governed by strict criteria, was found mainly in the supraoptic, paraventricular, and lateral nuclei. In the other nuclei, lesions either did not occur or were minimal. The distribution of severe neuronal damage in the paraventricular nuclei was not found in those cases of bulbar poliomyelitis which had not exhibited hyperthermia clinically. From this finding the authors conclude that the paraventricular group of nuclei plays an important part in the lowering of body temperature. Of the cases with hypothermia, 4 were accepted on similar rigid criteria, and in these severe histological lesions were found in the lateral and medial hypothalamic nuclei. As the lateral group is also affected in hyperthermia, only the medial group was deemed specific for the maintenance of normal body temperature. The posterior nuclear groups were not involved in any of the cases. The authors therefore consider that the posterior region of the hypothalamus has no influence on temperature regulation. *Ruby O. Stern*

911. **Cardiovascular Collagenosis with Parietal Endocardial Thrombosis. A Clinicopathologic Study of Forty Cases**

B. J. P. BECKER, C. B. CHATGIDAKIS, and B. VAN LINGEN. *Circulation* [*Circulation (N.Y.)*] **7**, 345–356, March, 1953. 8 figs., bibliography.

In a consecutive series of 9,500 necropsies performed between 1936 and 1951 at the University of the Witwatersrand, Johannesburg, 40 cases of endomyocardial necrosis and fibrosis with parietal endocardial thrombosis were found, 32 of which were in Bantus. The authors conclude from their histochemical findings in these cases that the condition is a form of collagenosis, the initial lesion being an acute or subacute focal degeneration of the ground substance of the endocardial connective tissues, followed in chronic cases by the formation of sclerotic endocardial plaques or by generalized fibrosis and increase of elastic tissue. Mural thrombi are frequently found overlying the fibrous plaques, occurring mostly in the left ventricle and the auricles. As a result of the detachment of portions of these thrombi visceral infarction occurs, chiefly in the lungs and kidneys. The majority of the myocardial lesions are found close to the endocardial lining and consist of areas of necrosis and fibrosis, possibly due to anoxia resulting from similar lesions in the subintimal tissues of the smaller blood vessels.

Although the lesions demonstrated are similar to those of acute collagenosis occurring elsewhere in the body, the authors consider that " the clinical picture and pathologic findings are sufficiently distinctive to warrant the recognition of this condition as a specific disease entity ". They propose for it the name " cardiovascular collagenosis with parietal endocardial thrombosis ".

G. J. Cunningham

912. **The Normal Glomerulus and Its Basic Reactions in Disease**

J. F. RINEHART, M. G. FARQUHAR, HAW CHAN JUNG, and S. K. ABUL-HAJ. *American Journal of Pathology* [*Amer. J. Path.*] **29**, 21–31, Jan.–Feb., 1953. 12 figs., 7 refs.

For histological examination of the normal glomerulus and of the glomeruli in nephritis, diabetes, hypertension, disseminated lupus erythematosus, and eclampsia, the authors, working at the University of California, used a colloidal iron preparation counterstained with cochineal and a combined iron and periodic-acid–Schiff stain. Kidney tissue perfused with osmic acid was also examined with the electron microscope. They distinguish between the endothelial and epithelial components of the basement membrane, and claim that the major component is a " differentiated cytoplasmic product of the endothelial cells ". The epithelial cells, on the other hand, produce a mucoid material which is spread over the basement membrane and penetrates it at regular intervals of about 0·12μ. *J. B. Enticknap*

913. **Glomerulonephritis**

D. B. JONES. *American Journal of Pathology* [*Amer. J. Path.*] **29**, 33–31, Jan.–Feb., 1953. 19 figs., 10 refs.

The changes in the glomerulus in the various stages of diffuse glomerulonephritis have been studied at the State University of New York, periodic acid and Gomori's silver methenamine stain being used on sections of necropsy material cut at 2μ. The author concludes that both the endothelial and the epithelial basement membranes exist and that in many disease conditions there is an accumulation of exudate in the potential interstitial connective-tissue space between them. In acute nephritis this often contains nuclei that are either fibroblastic or histiocytic, and thus the appearance of cellular glomeruli at this stage is due to infiltration with inflammatory cells rather than to endothelial cell proliferation. The degree of development of fibrous tissue in the glomerular scars in the chronic stage of the disease is related to the intensity of this initial exudate.

J. B. Enticknap

Bacteriology

VIRUSES

914. **Formation of the Particles of Influenza Virus**
R. W. G. WYCKOFF. *Journal of Immunology* [*J. Immunol.*] **70**, 187–196, Feb., 1953. 12 figs., 7 refs.

In seeking the origin of the spherical and filamentous forms of influenza-A virus, an examination by electron microscopy of infected cells was undertaken at the National Institutes of Health, Bethesda, Maryland. The micrographs obtained suggest that these particles develop not in the interior of the cells, but at the periphery, and are contiguous with the cell protoplasm. sometimes appearing as filaments with outlying single spheres. Evidence is given suggesting that the filaments, at first homogeneous, may split up into the spherical particles characteristic of influenza-A virus. Somewhat similar protrusions have been observed on cells infected with the Rous tumour virus and with vaccinia, but there is no evidence that these form the virus particles. It is therefore possible that the cytoplasmic change which results in the formation of protruding threads may be a non-specific cellular response to cellular injury.

R. Hare

915. **Growth of Poliomyelitis Viruses in Large Stationary Cultures**
C. A. MILLER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **82**, 450–454, March, 1953. 5 figs., 7 refs.

The roller tube technique for the propagation of the virus of poliomyelitis in tissue cultures has the advantage over earlier techniques of permitting direct examination of cultures and giving early growth of the virus, but has the obvious drawback of requiring the cultures to be rotated. In this report from the University of Kansas is described the successful growth of three strains (Brunhilde, Y-SK, and Saukett) in large stationary flask cultures of plasma-embedded monkey testis tissue.

Erlenmeyer flasks of 125 ml. capacity were first used, and yielded a supernatant fluid of high virus titre. Maximum growth occurred between the 3rd and 18th days, and the highest titres were obtained 9 or 10 days after virus inoculation. In view of this success, larger flasks were employed and the virus was successfully grown even in 6-litre rectangular culture bottles. However, the most manageable, and the least prone to mould contamination, were 1,000-ml. Roux flasks, along one side of which was spread 1 ml. of chicken plasma; this was then seeded with a fine mince of monkey testis until there were 8 to 12 fragments per sq. cm., when chick embryo extract was added to clot the plasma, 75 ml. of nutrient fluid containing penicillin and streptomycin was added, and the flask sealed and incubated at 35° C. The nutrient medium was changed every 3 days, and the virus (750 roller-tube infecting doses) was introduced at the second fluid change. All supernatant fluids were stored at −70° C. and cultures were discontinued 30 days after virus inoculation.

In 15 days a single Roux-flask culture yielded 300 ml. of supernatant fluid the virus titre of which was almost identical with that obtained in roller tubes. To obtain such a yield with roller tubes would have required 75 cultures.

D. Geraint James

916. **Poliomyelitis. I. Propagation of the MEF 1 Strain of Poliomyelitis Virus in the Suckling Hamster**
A. W. MOYER, C. ACCORTI, and H. R. COX. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **81**, 513–518, Nov., 1952. 1 fig., 15 refs.

The work described in these three papers from the Lederle Laboratories, Pearl River, New York, was undertaken with the object of obtaining a practical complement-fixation antigen for the diagnosis of poliomyelitis.

In the first series of experiments the MEF 1 strain of poliomyelitis virus was adapted to suckling hamsters by intracerebral inoculation. Two series of passages were carried out: the first (A) in 7- to 10-day-old suckling hamsters and the second (B) in 2- to 4-day-old hamsters. In both series the incubation period of the disease was shortened and the quantity of virus present, as measured by LD 50 titres in the mouse, gradually increased. At the 54th passage of the first (A) series, virus administered to 2 rhesus monkeys by intramuscular injection caused paralysis and death. At the 60th passage of the second (B) series, 7 rhesus monkeys received an intracerebral injection of the virus, and although one became paralysed and died, 6 escaped infection. In a similar experiment at the 64th passage, 2 out of 13 monkeys became completely paralysed, 2 had partial paralysis, and the remainder escaped infection.

In a further experiment 2 chimpanzees received by mouth 20% brain and cord suspensions from the 82nd, 84th, and 94th hamster passages of the (B) series. No virus was recovered from the stools and the animals remained free from symptoms; both animals developed neutralizing antibodies.

R. Hare

917. **Poliomyelitis. II. Propagation of MEF 1 Strain of Poliomyelitis Virus in Developing Chick Embryo by Yolk Sac Inoculation**
M. ROCA-GARCIA, A. W. MOYER, and H. R. COX. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **81**, 519–525, Nov., 1952. 1 fig., 24 refs.

In a second series of experiments [see Abstract 916] attempts were made to adapt the MEF 1 strain A of poliomyelitis virus to the developing chick embryo by yolk-sac inoculation. These were unsuccessful at the 70th, 80th, 100th, and 109th hamster passages, but at the

119th passage through suckling hamsters the virus could be propagated in the yolk sac of 7-day-old eggs following preliminary passage through Swiss albino mice. In this way the virus was maintained through 41 consecutive generations in developing eggs in one series, and through 38 generations in another series. The virus caused paralysis and death when administered to mice by intracerebral injection at each passage. That the virus thus passaged was the Lansing strain was demonstrated by neutralization tests in which anti-Lansing serum from three separate sources was used, by the ability of the passage virus to stimulate the formation of antibodies in monkeys, and by protection experiments in monkeys which had survived inoculation with the passage virus.

R. Hare

918. **Poliomyelitis. III. Propagation of MEF 1 Strain of Poliomyelitis Virus in Developing Chick Embryo by Allantoic Cavity Inoculation**

V. J. Cabasso, M. R. Stebbins, R. M. Dutcher, A. W. Moyer, and H. R. Cox. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **81**, 525–529, Nov., 1952. 1 fig., 13 refs.

In a third series of experiments [see Abstracts 916 and 917] the MEF 1 strain of the Lansing type of poliomyelitis virus was passaged in suckling hamsters, and at the 131st passage a 20% suspension of brain emulsion was injected into the allantoic cavity of 7-day-old chick embryos, the eggs being then incubated for a further 7 days. The virus survived and multiplied, as indicated by the results of inoculation of mice. In this way the virus was maintained through 40 successive passages in the allantoic cavity. In later experiments it was found that the titre was higher after 4 to 5 days' incubation than after 7 days. A second strain of the same virus, also propagated in suckling hamsters, was similarly found to be capable of multiplication in the allantoic cavity for 23 passages.

Intracerebral inoculation of the 13th-passage virus into 4 rhesus monkeys produced no symptoms in 3 and transient weakness of the hind legs in the fourth. At the 17th passage 8 monkeys were inoculated intracerebrally with the virus; no symptoms were observed in these animals or in 4 chimpanzees receiving the virus.

R. Hare

SEROLOGY AND IMMUNOLOGY

919. **A Serologically-active Erythrocyte-sensitizing Substance from Typhus Rickettsiae. I. Isolation and Titration**

S. Chang. *Journal of Immunology* [*J. Immunol.*] **70**, 212–214, March, 1953. 14 refs.

It has been shown by Keogh *et al.* (*Nature* (*Lond.*), 1947, **160**, 63, and 1948, **161**, 687) that certain complex polysaccharides derived from *Haemophilus pertussis* are easily and firmly adsorbed by erythrocytes, thus rendering the latter agglutinable by serum containing antibody against *H. pertussis*. This technique has since been applied to a number of bacteria possessing polysaccharide antigens, and the authors have succeeded in isolating a similar substance from *Rickettsia prowazeki*, the causative agent of typhus. The substance isolated is capable of sensitizing erythrocytes in the same manner and has therefore been named erythrocyte sensitizing substance (E.S.S.). The procedure for its isolation is described as follows.

Yolk sacs of chick embryos infected with Strain E of *R. prowazeki* are homogenized. This material should be sufficiently toxic to kill 50% of mice at a dilution of at least 1 in 30, or undesirable haemolytic properties derived from the yolk sacs may subsequently interfere with the tests. A 20% solution of the suspension in saline is centrifuged for an hour at 5,000 r.p.m. and the sediment resuspended in saline to the original volume of 20% solution. About 1 g. of celite per 6 g. of undiluted yolk-sac material is added, stirred for 5 to 10 minutes, and the celite removed by centrifuging at 1,000 r.p.m. for 10 minutes. Sufficient saturated sodium hydroxide solution to obtain a N/5 concentration is then added to the supernatant, which is heated in a boiling water bath for 30 minutes. The suspension is then dialysed overnight at 4° C. against isotonic phosphate–saline solution, when the E.S.S. remains in the bag as a turbid suspension. Haemolytic substances are still present in dilutions of this preparation up to 1 in 20, and are removed by shaking the suspension with an equal volume of chloroform for 20 minutes and centrifuging the mixture at 2,000 r.p.m. for 15 minutes. The purified E.S.S. remains in the clear aqueous phase.

E.S.S. does not give precipitin or complement-fixation reactions. It is standardized by determining the dilution which will completely sensitize a given volume of erythrocytes under standard conditions. Sensitization is carried out by adding 0·1 ml. of thrice-washed, packed, Group-O human erythrocytes to 4 ml. of E.S.S. dilutions and keeping the mixtures in a water bath at 37° C. for an hour. After sensitization the erythrocytes are washed twice and resuspended in saline. Erythrocytes sensitized in this way are agglutinated by sera containing typhus antibody. Complete sensitization is obtained when a higher concentration of E.S.S. does not increase the haemagglutination titre of a serum used in the titration. Qualitative tests showed that E.S.S. contains protein and probably carbohydrate.

K. S. Zinnemann

920. **A Serologically-active Erythrocyte-sensitizing Substance from Typhus Rickettsiae. II. Serological Properties**

S. Chang, J. C. Snyder, and E. S. Murray. *Journal of Immunology* [*J. Immunol.*] **70**, 215–221, March, 1953. 8 refs.

Sera from patients with epidemic typhus or Brill's disease, from healthy adults with residual typhus antibodies, from patients with non-rickettsial infections, and from animals immunized against *R. prowazeki* were all tested for the presence of typhus antibodies with E.S.S. prepared as described in the preceding paper [see Abstract 919]. The technique recommended is as follows. To 0·4 ml. of the various serum dilutions in Kahn tubes is added 0·1 ml. of sensitized erythrocytes.

Agglutinins against unsensitized human erythrocytes are excluded by means of a control tube containing 0·1 ml. of 1% washed, untreated, human Group-O erythrocytes and 0·4 ml. of a 1-in-10 dilution of test serum. The tubes are incubated for 16 to 22 hours at 30° C. and the agglutination pattern read in the usual way. Prozone reactions in dilutions up to 1 in 50 occur frequently.

The haemagglutination test carried out in this way shows that specific antibodies to E.S.S. are present in the serum of patients with typhus or Brill's disease in titres ranging from 1 in 10 to 1 in 60,000. The test does not distinguish between epidemic typhus and Brill's disease as the same E.S.S. apparently occurs in both. No E.S.S. antibodies were found in patients suffering from infections other than typhus (except for one Italian immigrant who may well have had an infection of the typhus group in childhood). The antibody against E.S.S., which appears 7 days after the onset of the disease, is not identical with the antibodies agglutinating *Proteus* X19 and typhus rickettsiae or with the complement-fixing antibody. The greatest advantage of the test is that it makes possible the detection of antibodies in serum from cases of Brill's disease, which often contains no agglutinins against *Proteus* X19. The test is simple to carry out and much more economical of material than the rickettsial agglutination test. *K. S. Zinnemann*

921. **Some Factors Influencing the Response of Animals to Immunisation with Combined Prophylactics**
M. Barr and M. Llewellyn-Jones. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **34**, 12–22, Feb., 1953. 17 refs.

In an investigation at the Wellcome Research Laboratories, Beckenham, Kent, guinea-pigs with an already established active immunity to diphtheria toxoid, and control animals, received injections of a prophylactic containing both diphtheria toxoid and tetanus toxoid, two doses being given at an interval of 28 days and the animals bled 10 days later. Three preparations were used, all containing 60 Lf of diphtheria toxoid per ml.; the content of tetanus toxoid was 6 Lf, 12·5 Lf, and 25 Lf per ml. in the three preparations respectively. Analysis of the resulting titres of antitoxin showed that interference with the tetanus response might occur even when diphtheria-immune animals were injected with a combined diphtheria–tetanus prophylactic of high tetanus-toxoid content.

Somewhat similar results were obtained when a prophylactic containing a vaccine and a toxoid (T.A.B. vaccine with tetanus toxoid) was employed. Guinea-pigs were given an injection of T.A.B. vaccine, followed at intervals of 28 days by two injections of T.A.B. vaccine with tetanus toxoid. Control animals received two injections of vaccine plus toxoid without the preliminary injection of vaccine. The results showed that those animals which had received a preliminary injection of vaccine responded with the lower antitoxin titres.

In another series of experiments T.A.B. vaccine was added to tetanus toxoid, and the antigenic efficacy of the mixture compared with that of tetanus toxoid alone. It was found that the addition of one particular batch of vaccine had no effect on the antigenic efficacy of tetanus toxoid, but with a different batch there was a significant reduction in the response when large doses were injected.

The authors conclude that while it is clearly desirable to give combined prophylactics for immunization, further investigation is required, since the results may depend on the relative proportions of the components, the dosage, the state of immunization of the subjects, and, in the case of a toxoid–vaccine preparation, the particular batch of vaccine used. *R. B. Lucas*

922. **Further Studies on Oral Administration of Living Poliomyelitis Virus to Human Subjects**
H. Koprowski, G. A. Jervis, T. W. Norton, and D. J. Nelson. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **82**, 277–280, Feb., 1953. 10 refs.

In an earlier investigation (*Amer. J. Hyg.*, 1952, **55**, 108; *Abstracts of World Medicine*, 1952, **12**, 8) 20 volunteers were given poliomyelitis virus orally, with the result that 16 patients, previously non-immune, developed neutralizing antibodies. In the present study, carried out in New York, 61 mentally deficient children aged from 8 months to 8 years, whose serum was found to contain no neutralizing antibody against the MEF 1 strain of Type-II poliomyelitis virus, were given orally the TN strain of rodent-adapted poliomyelitis virus in a dose of 5 ml. of a 20% suspension of infected cotton-rat brain and spinal cord. During the following 21 days the rectal temperature was taken 8-hourly and watch was kept for disturbances of the central nervous system. Stools were collected on 6 occasions for isolation of the virus, and samples of blood were taken for the same purpose every other day for 12 days. Blood was again taken 30 days after injection of the virus and subjected to a neutralization test.

None of the children showed any signs or symptoms which could be attributed to ingestion of the virus, nor was virus isolated from the blood in any case. However, virus was isolated from 53 specimens of faeces obtained from 29 of the 61 children, and neutralizing antibodies were present in the serum in 55 cases, significant quantities being detected in 52 of them.

Though 30 of the children showed evidence of pre-existing severe brain damage—a condition thought in the past to predispose to the paralytic form of poliomyelitis—in none did new neurological manifestations develop as a result of the experiment.

These results are held to confirm and to some extent amplify the observations made in the previous investigation referred to above. *R. B. Lucas*

923. **Experimental Researches into Anti-cellular and Anti-organic Sera : Parts 8 and 9.** (Sieri anticellule e antiorgano (Richerche sperimentali))
A. Cajano, C. Maurea, and A. Guarino. *Archivio "E. Maragliano" di patologia e clinica* [*Arch. "Maragliano" Patol. Clin.*] **8**, 285–316 and 317–346, March–April, 1953. 41 figs., bibliography.

Pharmacology

924. **An Assessment of Chlorophyll as a Deodorant**
J. C. BROCKLEHURST. *British Medical Journal* [*Brit. med. J.*] **1**, 541–544, March 7, 1953. 3 figs., 8 refs.

The results are reported of a number of experiments carried out *in vitro* at the University of Glasgow to determine the effect of chlorophyll on a number of substances with penetrating odours. Some clinical experiences are also described.

Methyl mercaptan gas was carried by nitrogen over a screen of filter paper soaked in chlorophyll solution or water in a closed system, and the amount of mercaptan passing beyond the filter paper measured by the reduction of a standard iodine solution. No absorption by the chlorophyll was detected, but the experimental error was large. No absorption was detected if the gas was bubbled slowly through chlorophyll solution and the amount measured as before. Chlorophyll did not abolish the odour of small quantities of mercaptan, ether, or syrup of garlic when each of these was placed in a small confined space with the solution ; nor did it deodorize small quantities of various strong-smelling solutions contained in stoppered test-tubes.

In a patient incontinent of urine and faeces, chlorophyll tablets in a dose of 400 mg. daily did not affect the odour of the urine. Another subject ate an average serving of asparagus after having taken 48 100-mg. tablets of chlorophyll during the preceding 24 hours; the characteristic odour of the urine was unaffected. A dose of 800 mg. of chlorophyll daily for one week did not remove the odour of faeces, urine, or axillary sweat.

Norval Taylor

925. **A Bacteriological Study of the Mode of Action of Chlorophyll as a Deodorant.** (Bakteriologischer Beitrag über den Wirkungsmechanismus des Chlorophylls bei der Desodoration)
E. v. WASIELEWSKI and A. ALBRECHT. *Zeitschrift für Hygiene und Infektionskrankheiten* [*Z. Hyg. InfektKr.*] **136**, 141–158, 1953. 45 refs.

Several theoretical mechanisms which would account for the deodorant properties claimed for preparations of chlorophyll are discussed, including adsorption, neutralization, and reduction of the offensive substance. In tests carried out at the University of Mainz the addition of 0·5 or 1% of a water-soluble chlorophyllin preparation had no qualitative or quantitative effect after 1 or 24 hours on the smell of several odoriferous substances, including skatol (concentration 10^{-6}), dodecylmercaptan (10^{-5}), and ammonia (10^{-4}), *in vitro*. It is suggested, however, that chlorophyll may act by preventing the formation of certain substances with an unpleasant smell rather than by destroying them, and experiments are described in which the addition of 0·05 to 0·2% of chlorophyllin reduced the odour of cultures of *Proteus vulgaris* grown on a medium containing egg-white, the smell of cultures containing chlorophyllin, independently tested by 8 observers, being less than that of control cultures after 24 hours' and again after 21 days' incubation. The effect of chlorophyll was not due to any difference in *p*H, and chemical tests confirmed that production of hydrogen sulphide, skatol, and ammonia by the chlorophyllin-containing cultures was depressed: indole production was less affected. The bacterial counts of cultures with and without chlorophyll differed only within the limits of experimental error.

Several experiments were carried out in order to study the action more precisely. Ammonia production by *Proteus* was reduced by 65 to 80% when 0·1% chlorophyll was present in media containing peptone or egg albumin. The effect on the production of hydrogen sulphide was absent in the presence of 0·05 to 1·0% of sodium pyrophosphate, which would combine with the magnesium in the chlorophyll. However, the deodorant effect appears to be a function of the whole chlorophyll molecule, and could not be reproduced by using magnesium chloride or magnesium-free components of the chlorophyll molecule. With a sterile extract of the proteolytic enzymes of *Proteus* and with peptone, alanine, or leucyl-glycyl-glycine as substrate it was shown that chlorophyll reduced amino-acid breakdown. Chlorophyll thus appears to inhibit *in vitro* the activity of certain proteolytic bacterial enzymes.

Derek R. Wood

926. **Capacity of a Cationic Exchange Resin (" Zeo-Karb 225 ") *in vivo***
P. FOURMAN. *British Medical Journal* [*Brit. med. J.*] **1**, 544–546, March 7, 1953. 9 refs.

In three balance experiments a cationic exchange resin (" zeo-karb 225 ") was given in H or NH_4 form to 2 normal persons in a daily dose of 60 and 90 g. The diets contained about 200 mEq of Na, 31–38 mEq of K, and 12–22 mEq of Mg. With either form of resin and with both doses the resin took up Na, K, and Mg in a fairly constant ratio of about 11 : 5 : 1. Ca was not taken up. The amount of Na taken up by the NH_4 form was about 2 mEq/g.

In three patients with a low intake of Na the amount of Na taken up was only 0·7 mEq/g., and was further diminished when K was added to the treatment.

The capacity of the resin *in vivo* was estimated from the change in faecal excretion of cations and also, for the NH_4 form, from the change in faecal N. The capacity of the two forms of resin *in vivo* approached their capacity *in vitro*; that of the NH_4 form was about 3 mEq/g. *in vivo*.

With resin, the change in daily excretion of acid and ammonia in the urine was approximately the same as the change in excretion of cations in the faeces.

The results suggest methods of assessing the capacity of the resin *in vivo*. The capacity of the resin *in vivo*

and the proportions of Na, K, Mg, and Ca that combine with the resin may well vary with the amounts of Na, K, Mg, and Ca in the intestine.—[Author's summary.]

927. **The Effect of Nikethamide by Mouth in Man**
J. G. MACARTHUR. *British Medical Journal* [*Brit. med. J.*] **1**, 547, March 7, 1953. 15 refs.

Nikethamide was administered orally in doses of 5 ml. and 10 ml. five times daily, and in single doses of 16 ml. and 30 ml. It produced no effects on the cardiovascular or respiratory system. When symptoms and signs of cardiac failure were present they were not affected by the treatment.—[Author's summary.]

928. **Clinical Trial of Phenylindanedione as an Anticoagulant**
M. TOOHEY. *British Medical Journal* [*Brit. med. J.*] **1**, 650–652, March 21, 1953. 6 refs.

Of the anticoagulant drugs at present available for administration over long periods in the treatment of thrombo-embolic disease, dicoumarol has the disadvantage of cumulative action, necessitating frequent estimations of the prothrombin time if severe haemorrhage is to be avoided; a further disadvantage is the delay of 48 to 72 hours before the full therapeutic effect is obtained. Ethylbiscoumacetate (" tromexan ") on the other hand is effective within 18 to 24 hours, but while its rapid metabolism and elimination ensure that a cumulative effect is rarely produced, they also make it difficult to maintain a steady therapeutic blood prothrombin level, and wide individual fluctuations in response frequently occur, necessitating meticulous laboratory control. The newly introduced anticoagulant phenylindanedione lies midway between dicoumarol and ethylbiscoumacetate in that the dangerous cumulative action of dicoumarol is rarely seen, while it is less rapidly eliminated than ethylbiscoumacetate, making clinical control easier.

Phenylindanedione was used at New End Hospital, London, in the treatment of 68 patients, most of whom were suffering from coronary thrombosis or deep venous thrombosis. The majority received 200 mg. of phenylindanedione in the first 24 hours followed by 100 mg. in the next 24, at the end of which the blood prothrombin level had been reduced to an adequate therapeutic level (10 to 20% of normal) in all but 6 cases. A prothrombin estimation was carried out after the first 24 hours and the second dose reduced if necessary. The maintenance dose lay between 75 and 100 mg. daily in 44 cases, and in only 5 cases did it fall outside the range of 50 to 150 mg.; it was given in two equal parts, night and morning.

In general it is noted that the more robust and younger patient requires a large maintenance dose, while the seriously ill, frail, elderly patient needs a smaller dose. Much smaller doses are required where renal function is depressed, and it was found useful to perform blood urea estimations as a routine on all patients of 60 and over. As phenylindanedione is very uniform in its action it is sufficient, once the maintenance dose has been determined, to carry out prothrombin estimations only twice or at the most three times a week. In the very few cases in which the prothrombin time failed to return to normal within 48 to 72 hours of stopping treatment there were signs of deficient renal function. Vitamin K_1, given by mouth, is a rapid and effective antidote. No side-effects of phenylindanedione were noted.

Robert Hodgkinson

929. **Clinical Experience with a New Indandione Derivative: a Preliminary Report**
I. F. DUFF, E. W. DENNIS, P. E. HODGSON, and W. W. COON. *University of Michigan Medical Bulletin* [*Univ. Mich. med. Bull.*] **19**, 43–48, Feb., 1953. 5 figs., 3 refs.

The effect on prothrombin time of a new indanedione derivative, " dipaxin " (2-diphenylacetyl-1 : 2-diketohydrindene), has been investigated at the University of Michigan Medical School, Ann Arbor. Dipaxin resembles phenylindanedione in the speed with which it produces a therapeutic effect, but the duration of this effect after administration of the drug is discontinued is somewhat longer than that of phenylindanedione. Weight for weight, dipaxin is more potent than phenylindanedione, the effective initial dose being 30 to 75 mg. and the maintenance dose 5 to 30 mg. or less daily. Vitamin K_1 is a rapid and effective antidote to dipaxin. No toxic effects from the use of this new drug were encountered.

A. Brown

930. **The Effect of Newer Anticholinergic Drugs upon Gastric Secretion in Man**
J. B. KIRSNER, E. LEVIN, and W. L. PALMER. *Gastroenterology* [*Gastroenterology*] **23**, 199–218, Feb., 1953. 2 figs., 30 refs.

In this detailed report from the Frank Billings Medical Clinic, University of Chicago, six anticholinergic substances are compared for their activity in depressing gastric secretory activity in man, namely, methantheline (" banthine ") and " prantal " (N:N-dimethyl-4-piperidylidene-1:1-diphenylmethane methyl sulphate), and four new compounds designated A.P. 193 (diethylaminoethyl-β-hydroxy-α-phenyl*cyclo*hexane acetate), U.0407 (pyrrolidylethylphenyl*cyclo*pentenyl acetate ethobromide), U.0385 (diphenyl-(2-piperidylethyl)-acetamide methobromide), and U.0229 (α:α-diphenyl-γ-(1-piperidyl)-butyramide hydrochloride). The first of the 4, A.P.193, was less fully studied than the others, because of its relatively low activity and undesirable side-effects. In 359 tests of basal gastric secretion, 215 in patients with peptic ulcer and 144 in normal volunteers, during which mydriasis, heart rate, and blood pressure were also investigated, particular attention was given to the influence of route of administration, dosage, and toxicity of the drugs.

After intramuscular injection the five compounds (excluding AP.193) caused significant reduction of output of acid. Absence of free acid for at least 30 minutes (anacidity) occurred after a latent period of 15 minutes after injecting 1·2 to 2·0 mg. of U.0229, 1·6 to 2·0 mg. of U.0385, or 15 to 20 mg. of banthine. Effective doses of U.0229 and U.0385 had a more prolonged action than banthine. After 50 mg. of prantal and 6 to 10 mg.

of U.0407, the volume of secretion was always reduced, and anacidity occurred in 4 and 3 respectively of the 5 subjects tested with each substance at these dose levels. The decreasing order of potency was found to be U.0229, U.0385, banthine, U.0407, and prantal.

Oral administration was much less effective and, except with U.0229, much larger doses were required to produce any action at all. For example, banthine by mouth in doses sufficient to produce side-effects never produced anacidity, and AP.193 was totally ineffective. Repeated injection or slow intravenous infusion of U.0229 caused a long-lasting anacidity. Given intraduodenally the drugs had a greater effect than when similar doses were given orally. Intramuscular injection of doses capable of suppressing basal secretion did not effectively inhibit the secretion of acid in response to the histamine analogue, 3-β-aminopyrazole, in 34 experiments. The possibility of finding an anticholinergic substance with a relatively selective action on gastric secretion is briefly reviewed and an interesting diagram is given showing how far these substances satisfied the criteria of prolonged anacidity with minimal side-effects. It is concluded that these drugs vary greatly in their effects on gastric secretion and in producing side-effects, and that they are generally much less effective by mouth, although U.0229 and U.0385 do depress gastric acidity by this route. These two, however, which were the most effective secretory depressants, produced side-effects more often than less effective compounds.

[This report indicates that some progress may have been made in the search for a selective and effective gastric secretory depressant among anticholinergic drugs but, as is stressed, there is wide variation in individual response both in terms of secretory inhibition and incidence of side-effects. Further experience may show how certain such progress is.] *Derek R. Wood*

931. **Newer Gastric Antisecretory Compounds**
J. B. KIRSNER and W. L. PALMER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 798–805, March 7, 1953. 2 figs.

The various criteria which may be used in evaluating the gastric antisecretory potency of drugs are reviewed, comparisons based on the average reduction in volume and acidity of the gastric juice in groups of patients and on the changes occurring in the individual subject being regarded by the authors as equally unsatisfactory. They therefore assessed the relative clinical value of 16 antisecretory compounds at the University of Chicago on the basis of the incidence and duration of gastric anacidity and the incidence and severity of side-effects after administration of the drugs to persons secreting moderate or large amounts of acid gastric juice—mostly patients with duodenal ulcer.

The drugs tested included belladonna, atropine, hexamethonium bromide, " prantal ", " pamine ", " anthenyl " (oxyphenonium bromide), " pro-banthine " (propantheline), " darstine ", and compounds distinguished by the serial numbers U.0407, U.0385, U.0229, Ap.407, Win.4369, 14045, 1637, and B.L.139. [These compounds are all parasympathetic inhibitors of varying chemical structure, for details of which the original paper should be consulted.]

Five of these compounds were administered intramuscularly, and each produced anacidity of varying duration; in order of decreasing potency they were pamine, U.0229, U.0385, U.0407, and prantal. The most potent antisecretory compounds on intragastric administration were U.0229, pamine, Win.4369, U.3085, and pro-banthine, but it was found that those compounds which most completely inhibited gastric secretion also produced the most side-effects; pamine, pro-banthine, and Win.4369, given in single doses, produced the least troublesome reactions, although there were wide individual variations in the occurrence and severity of reactions to the same dose given on different occasions.

Robert Hodgkinson

932. **Pharmacology of M. & B. 2050**
R. WIEN and D. F. J. MASON. *Lancet* [*Lancet*] **1**, 454–455, March 7, 1953. 2 refs.

The pharmacology of a new compound, " M and B 2050 ", the di-iodide of pentamethylene-1:5-bis-N-(N-methyl-pyrrolidinium) is described. It is about five times more potent than hexamethonium bromide in paralysing ganglionic transmission, and it acts for 1½ times longer. This was shown by experiments on the superior cervical ganglion of the cat, in which post-ganglionic excitation or the injection of adrenaline remained fully effective during the complete inhibition of preganglionic excitation. The bradycardia and fall in blood pressure on vagal excitation were abolished, whereas the depressor effect of acetylcholine remained unchanged.

The new compound has a hypotensive action which is similar to that of hexamethonium, although the onset is slower and the recovery more prolonged. It is devoid of anticholinesterase, neuromuscular-paralysing, and histamine-liberating properties when given in doses fully effective in blocking ganglia, and it appears to have no direct effect on the heart. In rats and guinea-pigs the growth rate, blood picture, and bodily health were not affected by daily subcutaneous injections for 2 to 4 weeks of doses far in excess of those pharmacologically effective. *G. B. West*

933. **Action of a New Methonium Compound in Arterial Hypertension. Pentamethylene-1 : 5-bis-N-(N-methyl-pyrrolidinium) Bitartrate (M. & B. 2050A)**
F. H. SMIRK. *Lancet* [*Lancet*] **1**, 457–464, March 7, 1953. 5 figs., 11 refs.

The results here reported from Otago University School of Medicine, New Zealand, were obtained with the new compound " M and B 2050A " which is the bitartrate salt of pyrrolidinium corresponding to the di-iodide, " M and B 2050 " [see Abstract 932]. It was administered by subcutaneous injection and by mouth and its effect compared at all stages with that of hexamethonium bromide. In hypertensive patients in the sitting posture an initial subcutaneous dose of 15 mg. of hexamethonium induced a distinct fall of blood pressure which was comparable with that produced

by 3 mg. of compound M and B 2050A. Whereas the effective oral dose of hexamethonium was from 350 to 2,100 mg., much smaller doses of the new compound were required. In 10 patients who had developed some tolerance, the range of dosage of hexamethonium given by mouth was 250 to 1,500 mg.; in 11 patients similarly treated, the range of oral dosage of M and B 2050A was 100 to 700 mg. Side-effects were less when the dose was small. Repetition of an effective subcutaneous dose of M and B 2050A within 4 hours led to an exaggerated fall of blood pressure. Oral doses of this compound administered before breakfast needed only a small additional dose before lunch to extend the period of activity into the early evening. Evidence of cross-tolerance to the two drugs was found.

In extended clinical trials, 15 patients receiving continuous subcutaneous treatment with M and B 2050A for periods ranging from 8 to 19 weeks suffered no serious side-effects. Satisfactory results were obtained with simple 2% aqueous solutions containing 0·5% chlorbutol as an antiseptic. When the compound was dissolved in 25% polyvidone solution (containing ephedrine), a single injection produced a fall of blood pressure lasting 8 to 12 hours, only 2 injections being required daily. In another series, 14 patients were successfully treated by oral administration of M and B 2050A for periods ranging from 8 to 14 weeks, and no important side-effects were noted. The initial trial dose was 20 mg., and this was raised by 20 mg. daily until the desired effect was attained.

Although the control of dosage presents some new problems, the author considers that M and B 2050A should prove superior to hexamethonium bromide for oral administration. Preliminary studies justify extensive therapeutic trials of this compound given both orally and subcutaneously. *G. B. West*

934. **New Sympathicolytic Agents**

R. D. H. Maxwell and A. J. M. Campbell. *Lancet* [*Lancet*] **1**, 455–457, March 7, 1953. 2 figs., 19 refs.

A series of 9 new ganglion-blocking compounds, structurally related to hexamethonium, have been tested in man and their actions compared with those of hexamethonium and its monoethyl homologue (" gaplegin "). Subcutaneous doses were first determined which definitely lowered the blood pressure of 75 normal subjects (sympathicolytic action) and produced achlorhydria in the fasting gastric secretion (vagolytic action). The effects of hypotensive doses of all 11 compounds in producing mydriasis (vagolytic action) and an alteration in peripheral circulation (sympathicolytic action) were then measured. In these tests, " M and B 1950 " (phenyldimethonium) and " M and B 2050 " (pentapyrrolidinium) had the highest sympathicolytic activity.

These two drugs were therefore given at the Royal Alexandra Infirmary, Paisley, to 15 patients with hypertension, of whom 10 had previously been treated with hexamethonium by parenteral and oral administration. The effect of a single dose was first studied and compared with those of hexamethonium and control doses of sterile water. Then 50 subcutaneous injections in doses varying between 2·5 and 50 mg. of each drug were given, and subsequently the effects of 50 oral doses of 25 to 150 mg. of each were recorded. The two new drugs produced hypotension when given subcutaneously in a dosage which was about one-fifth of the amount of hexamethonium required to produce a comparable fall in blood pressure. Pentapyrrolidinium was found to be the more active of the two, but it was less selective in action, mydriasis and dryness of the mouth being invariably produced. The action of these new drugs lasts longer than that of hexamethonium, and more consistent results follow oral administration. Headache, drowsiness, and depression in some cases were the only side-effects of pentapyrrolidinium, but their incidence and severity in no case necessitated withdrawal of the drug.

A warning is given that the high activity of these compounds may produce severe hypotension, and caution in their administration is necessary.

G. B. West

935. **Analgesic and Other Properties of 3 : 3-Dithienylalkenylamines**

A. F. Green. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **8**, 2–9, March, 1953. 5 figs., 12 refs.

Powerful analgesic properties and some atropine-like, antihistamine, and local anaesthetic properties have been found in a series of 3 : 3-dithienylalkenylamines. 3-Dimethylamino, 3-ethylmethylamino, 3-diethylamino, 3-pyrrolidino, and 3-piperidino-1 : 1-di-2′-thienylbut-1-ene hydrochloride show activities varying between 0·6 and 1·7 times that of morphine sulphate in rats and rabbits, and between 0·1 and 0·4 times that of morphine in dogs and cats. The ethylmethylamino compound is the most active. Compared with morphine, their respiratory and temperature depressant activities are proportional to their analgesic potencies, but they seem to have less effect on the bowel. In this and other respects they and pethidine have a similar type of action, differing from that of morphine and amidone.

The *dextro* isomerides of the dimethylamino and pyrrolidino compounds exhibited greater analgesic, antihistamine, and atropine-like properties than the *laevo* isomerides.—[Author's summary.]

936. **The Analgesic and Antipyretic Action of the Combination of Acetophenetidin and Barbital.** [In English]

L.-O. Boréus and F. Sandberg. *Acta physiologica Scandinavica* [*Acta physiol. scand.*] **28**, 6–13, March 31, 1953. 3 figs., 7 refs.

The influence of three hypnotic drugs, barbitone, 1-benzyl-5-allyl*iso*propylbarbituric acid, and carbromal, on the analgesic and antipyretic actions of phenacetin (" acetophenetidin ") was studied in rats at the Karolinska Institute, Stockholm. Each of the hypnotic drugs was given by mouth with phenacetin in the ratio of 1 : 3, three dose levels being used, namely, 80+240, 40+120, and 20+60 mg. per kg. body weight. To determine the analgesic effect of the various drug combinations, the time taken for the animals to respond to the appli-

cation of heat of constant intensity to a fixed area of the shaved back was measured. The antipyretic action was determined by ascertaining the reduction in temperature in rats with fever which had been induced by the subcutaneous injection of yeast suspensions 14 to 15 hours before administration of the drugs. In each case the values were estimated at intervals of one hour for 4 hours after administration of the drugs. The significance of the maximum effect (as measured in a pilot experiment) was determined for the analgesic action one hour after the drugs had been given and for the antipyretic effect three hours after the drugs had been given at the highest dose level and two hours after they had been given at the two lower dose levels.

Each of the hypnotic drugs reduced the analgesic action of phenacetin. The reduction of the analgesic action by barbitone and by 1-benzyl-5-allyl*iso*propylbarbituric acid was significant at the two lower dose levels but not at the highest level. Carbromal reduced the analgesic action significantly at the two higher dose levels but not at the lowest dose level. The influence of the hypnotics on the antipyretic action of phenacetin was less clear-cut. There was no synergism between phenacetin and barbitone or carbromal, but 1-benzyl-5-allyl-*iso*propylbarbituric acid enhanced the antipyretic effect at the two higher dose levels. Carbromal antagonized the antipyretic effect only at the lowest dose level.

P. A. Nasmyth

937. **Some Morphine-like Properties of (±)-*cyclo*-Hexyloxy-*alpha*-phenylethylamines**
A. McCoubrey. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **8**, 22–25, March, 1953. 1 fig., 17 refs.

m- and *p-cyclo*Hexyloxy-α-phenylethylamine show qualitative similarity to morphine in analgesic activity, respiratory depression, effect on body temperature and blood pressure. No consistent response was obtained for blood sugar changes.

m- and *p-iso*Propyloxy- and *p*-ethoxy-α-phenylethylamine have no analgesic activity and, apart from respiratory depression, their pharmacological properties are different from those of the *cyclo*hexyl ethers and morphine.

Evidence was obtained to show that the analgesic effect of the *cyclo*hexyloxy-α-phenylethylamines is more nearly related to that of morphine, amidone, and pethidine than to the chemically analogous antipyretic and analgesic phenacetin.—[Author's summary.]

938. **The Response of Circulating Eosinophile Cells to Morphine and Related Substances**
J. C. Szerb. *Canadian Journal of Medical Sciences* [*Canad. J. med. Sci.*] **31**, 8–17, Feb., 1953. 8 figs., 27 refs.

In order to investigate the possibility of adrenocorticoid hormones being released by narcotic drugs, the action of morphine, " meperidine " [pethidine], and codeine on the number of circulating eosinophile cells was determined. In mice 10 mg. per kg. of morphine caused a significantly greater drop in the number of eosinophiles two hours after the injection than did 20 mg. per kg. of histamine. Adrenalectomy prevented the decrease following the injection of morphine and histamine. The comparison of the action of 10 mg. per kg. of morphine, 20 mg. per kg. of meperidine, and 30 mg. per kg. of codeine showed the greatest decrease in the number of eosinophiles after meperidine and the smallest after codeine. In humans 10 mg. of morphine caused the largest (about 50%) decrease in the circulating eosinophiles followed by 50 mg. of meperidine and 30 mg. of codeine. The maximal fall occurred two hours after the injection. The possible mechanism of the action of narcotic drugs on the pituitary–adrenocortical system is discussed.—[Official abstract.]

939. **Study of the Mercurial Diuretic, Dicurin Procaine (Merethoxylline Procaine) by Subcutaneous Injection**
M. M. Best, W. F. Hurt, J. E. Shaw, and J. D. Wathen. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **225**, 132–138, Feb., 1953. 1 fig., 5 refs.

Many attempts have been made to develop a non-irritant organic mercurial diuretic which may be given subcutaneously. The study here reported was carried out at the Institute for Medical Research, University of Louisville, Kentucky, on 69 oedematous patients who were given a total of 540 subcutaneous injections of a new mercurial compound—merethoxylline procaine with theophylline (" dicurin procaine "), having the formula sodium-*o*-(N-hydroxy-mercuri - methoxyethoxy) - propylcarbamyl phenoxyacetate procaine.

Its diuretic efficacy was found to resemble that of mercaptomerin sodium, but local reactions were frequent, 20% of the patients having pain of more than 8 hours duration, subcutaneous nodule formation, and areas of ecchymosis at the site of injection. Nevertheless, the authors declare themseives satisfied with this new compound as a diuretic.

[In an addendum to the paper they report the giving of a further 428 injections, with similar results.]

G. B. West

940. **A Study of the Therapeutic Efficacy of Phenylbutazone (" Butazolidin ").** (Estudio sobre la efectividad de butazolidina)
P. Barceló and A. Serra-Peralba. *Medicina clínica* [*Med. clín. Barcelona*)] **20**, 152–161, March, 1953. 3 figs., 23 refs.

At the University Medical Clinic, Barcelona, 25 patients with rheumatoid arthritis were treated with phenylbutazone given orally or by injection. The results were good, 14 patients obtaining complete and 7 partial relief. The beneficial effect was apparent within 3 hours, and the drug appeared to act by damping down the inflammatory process rather than solely by virtue of its analgesic properties. Its action also appeared to be more prolonged than that of cortisone. Severe toxic effects were not encountered in this small series of cases, but malaise, skin rashes, epigastric pain, and buccal ulcers were noted. The authors conclude that phenylbutazone is a valuable drug for the treatment of the acute phases of rheumatoid arthritis. *K. Gurling*

Chemotherapy

941. **Proguanil—the Isolation of a Metabolite with High Antimalarial Activity**
A. F. CROWTHER and A. A. LEVI. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **8**, 93–97, March, 1953. 18 refs.

The authors report the isolation of a highly active metabolite of proguanil, a dihydrotriazine, from the urine and faeces of rabbits and from the urine of human volunteers after administration of the drug. [For details of the chemical structure of the two substances the original paper should be consulted.] The yield from human urine (based on the dose of proguanil given) was about 5%. The metabolite, which was also synthesized by the authors, was considerably more active than proguanil against the malaria parasite, being 10 times more effective against *Plasmodium gallinaceum* in chicks, and it was also active against the exo-erythrocytic forms. Since the antimalarial activity of the metabolite was of a type similar to that of proguanil, it was concluded that proguanil owed its effectiveness against malaria to the formation of the metabolite within the body. It was therefore to be expected that other active diguanides would undergo a similar metabolic change. This was confirmed by administering the most potent compound of the diguanide series, N^1-3 : 4-dichlorophenyl-N^4-*iso*propyldiguanide, to rabbits and extracting from the urine a dihydrotriazine which was found to be 10 times more active than the proguanil metabolite, and consequently 100 times more so than proguanil itself, against the blood forms of *P. gallinaceum* in chicks.

R. Wien

942. **Treatment of Urinary Tract Infections with a New Antibacterial Nitrofuran**
S. MINTZER, E. R. KADISON, W. H. SHLAES, and O. FELSENFELD. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **3**, 151–157, Feb., 1953. 4 refs.

The authors report the trial at Cook County Hospital, Chicago, of a new chemotherapeutic drug—"furadantin" (nitrofurantoin ; N-(5-nitro-2-furfurylidene)-1-aminohydantoin), and point out that the nitrofurans in general offer stability, a wide antibacterial spectrum, and little tendency to the development of bacterial resistance.

They found that absorption of the drug following oral administration is practically complete: about 45% is excreted in the urine, but blood levels are extremely low. A state of stable supersaturation can exist in the urine, and this suggests that crystalluria need not be feared. The antibiotic is effective against many Gram-negative and Gram-positive bacteria and certain protozoa *in vitro* and *in vivo*. It is not effective against rickettsiae, viruses, or fungi *in vitro*. Combination of furadantin with penicillin or streptomycin has definite synergistic effects *in vitro*.

With the recommended dosage of 5 to 7 mg. per kg. body weight, nausea occurred in only 2 of 59 patients. On a higher dosage of 10 to 12 mg. per kg. body weight 6 of 25 subjects had nausea and one vomited.

Furadantin was administered to 12 patients with urinary infections who had previously been unsuccessfully treated with sulphonamides, penicillin, and streptomycin, good results being obtained in 8 of these cases. The authors conclude that this drug appears to offer much promise in the treatment of bacterial urinary infections.

A. W. H. Foxell

943. **Researches into the Mode of Action of Modern Chemotherapeutic Drugs on *Mycobacterium tuberculosis*, with Special Reference to Natural (Non-specific) Phagocytosis.** (Untersuchungen über die Einwirkung moderner Tuberkulose-Therapeutica auf *Mycobacterium tuberculosis* unter besonderer Berücksichtigung der natürlichen (unspezifischen) Phagocytose)
W. SCHMIDT. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **108**, 227–236, Jan. 31, 1953. 4 figs., 7 refs.

The mode of action of 3 chemotherapeutic agents used in the treatment of tuberculosis was investigated at the Justus Liebig Hochschule, Giessen, and their effect on phagocytosis particularly studied. A fine suspension of tubercle bacilli was mixed with washed guinea-pig leucocytes in a test tube, and the degree of phagocytosis observed after the addition of each drug. It was found that streptomycin and PAS both caused a threefold increase of phagocytosis as compared with controls when kept in contact with tubercle bacilli for at least 24 hours at 37° C. A greater degree of phagocytosis was produced when the drug and the tubercle bacilli were kept in contact for longer periods. "Conteben" (thiacetazone) caused only a slight increase in phagocytosis under the same conditions. The mode of action *in vivo* was also investigated, guinea-pigs being infected by the intraperitoneal injection of tubercle bacilli and estimations of the degree of phagocytosis carried out on specimens of peritoneal fluid after treatment with each of the drugs. It was found that treatment with streptomycin and PAS produced only a slight increase in phagocytosis, whereas a marked increase occurred on treatment with thiacetazone.

Robert Hodgkinson

944. **Withdrawal Symptoms upon Discontinuance of Iproniazid and Isoniazid Therapy**
I. J. SELIKOFF, E. H. ROBITZEK, and G. G. ORNSTEIN. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 212–216, Feb., 1952. 9 refs.

The authors have studied the withdrawal symptoms which followed the discontinuance of treatment with iproniazid and isoniazid in a group of 65 patients receiving these drugs for periods of 16 to 44 weeks at Sea View Hospital, New York. The symptoms, which consisted in the main of headache, nightmares, vertigo, nervousness, hyperreflexia, insomnia, irritability, and

depression, occurred in two-thirds of the patients treated with iproniazid, but in a much smaller proportion of patients who had received isoniazid. They appeared within 24 to 48 hours of discontinuance of the drug and in some instances persisted for as long as 6 weeks, although in most cases they abated markedly after 1 week and had disappeared in 2 weeks. Gradual withdrawal of the drug diminished the severity and frequency of the symptoms, but did not entirely eliminate them. No symptoms were observed in patients receiving treatment for less than 6 weeks. *R. H. J. Fanthorpe*

ANTIBIOTICS

945. **The Bactericidal Action of Isoniazid, Streptomycin, and Terramycin on Extracellular and Intracellular Tubercle Bacilli**

G. B. MACKANESS and N. SMITH. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 322–340, March, 1953. 13 figs., 40 refs.

No antituberculous drug at present available will eliminate all tubercle bacilli from experimentally infected animals, organisms still being recoverable from tissues after prolonged treatment with streptomycin and isoniazid. Three possible explanations are offered: (1) development of resistance by the organism; (2) the bacilli may be so situated that the drug cannot reach them; (3) some of the bacilli may be in a metabolic state in which they are not susceptible to the drug. In experiments performed at the Sir William Dunn School of Pathology, Oxford, the survival of tubercle bacilli when exposed to isoniazid, streptomycin, and oxytetracycline (terramycin), singly or in combination, and their survival in living macrophages similarly exposed were studied.

The H37Rv strain of *Mycobacterium tuberculosis* was used, and inocula were taken from shallow cultures in Dubos–Davis medium containing 0·05% "tween 80" and 0·25% heat-inactivated bovine albumin Fraction V, shaken daily and harvested after 11 days. Concentrations of streptomycin varied from 100 to 0·1 μg. per ml. and of isoniazid from 10 to 0·01 μg. per ml. In the combination of the drugs 0·1 μg. of isoniazid was added to the streptomycin series, and 1·0 μg. of streptomycin to the isoniazid series. A special technique of counting viable organisms was applied at the beginning and after 12 hours and 1, 2, 4, 8, 18, and 32 days at 37° C. All cultures thought to be free of viable organisms were checked by guinea-pig inoculation. Macrophages from normal rabbits containing an average of 5 tubercle bacilli per cell were exposed to culture media containing 100, 10, or 1 μg. of streptomycin per ml., 10, 1·0, and 0·1 μg. of isoniazid per ml., and the same amounts of streptomycin and isoniazid combined.

Results showed that a concentration of 10 μg. of isoniazid per ml. was not uniformly bactericidal and 1·0 μg. streptomycin per ml. was not inhibitory, but that 1·0 μg. of streptomycin with 0·01 μg. of isoniazid per ml. was. The death rate of the tubercle bacilli varied directly with the drug concentration. Survival curves of bacilli exposed to isoniazid showed a delay of 48 hours before the onset of any fall in viable count. Simultaneous exposure to both drugs gave a consistent deflection equal to the effect produced by about 10 times the concentration of either alone. The bactericidal action of oxytetracycline was small at 10 μg. per ml. and its combination with isoniazid completely inhibited the bactericidal action of isoniazid.

In living macrophages, 25 μg. of streptomycin per ml. was necessary to inhibit intracellular tubercle bacilli, but 1 μg. of isoniazid per ml. was adequate. Cultures died after 5 days' exposure to inhibitory concentrations. The effect of 10 μg. of streptomycin and 1 μg. of isoniazid per ml., singly and in combination, was studied; streptomycin alone gave an insignificant reduction in the number of infected macrophages, but when combined with isoniazid, sterile cultures were obtained within 11 days, the combination accelerating the death rate; for example, after 4 days the number of survivors in presence of the two inhibitors was about half that in either alone.

The authors conclude that relatively high concentrations of streptomycin are needed with isoniazid to obtain a potentiation of bactericidal activity against intracellular tubercle bacilli owing to the poor penetrability of streptomycin. It is suggested that isoniazid is likely to be more effective than PAS in controlling streptomycin-resistant variants because of its greater lethal power against intracellular organisms. *Malcolm Woodbine*

946. **Antibiotic Resistance of Pathogenic Staphylococci. Study of Five Hundred Strains Isolated at Boston City Hospital from October, 1951, to February, 1952**

M. FINLAND and T. H. HAIGHT. *Archives of Internal Medicine* [*Arch. intern. Med.*] **91**, 143–158, Feb., 1953. 1 fig., 48 refs.

The occurrence of resistant staphylococci was observed shortly after the introduction of penicillin in 1940, and since that time the increasing incidence of penicillin-resistant strains of this micro-organism has been repeatedly noted. The close correlation between penicillin resistance and penicillinase production has been pointed out, but no correlation has been found between the latter and haemolysis, pigment production, or coagulase activity. Furthermore, it has been observed that whereas different strains of staphylococci vary widely in their resistance to penicillin, they are uniformly sensitive to other antibiotics.

The aim of the present study, which was carried out at the Boston City Hospital, was to evaluate the sensitivity of strains of staphylococci isolated between October, 1951, and February, 1952, to the antibiotics now in general use. Some 500 strains have been examined—185 from the respiratory tract, 124 from skin, 57 from abscesses, 41 from cases of osteomyelitis, 35 from urine, 33 from faeces, and 25 from blood. The sensitivity of these strains was determined by a serial twofold agar-plate dilution method, and tests for penicillinase production were carried out. The results of the sensitivity tests, in which 9 antibiotics were used, indicated a wide range for penicillin, aureomycin, and oxytetracycline (terramycin). Distribution curves for streptomycin, neomycin, chloramphenicol, and polymyxin B showed

less variation and, especially for erythromycin, no naturally occurring staphylococci of high or moderate resistance were encountered. Similar results have recently been reported for magnamycin (carbomycin). Weight for weight, the order of effectiveness was: erythromycin, aureomycin, oxytetracycline, bacitracin, streptomycin, chloramphenicol, neomycin, polymyxin B, and penicillin, but about 20% of the strains were more sensitive to penicillin than the rest. The strains were graded arbitrarily, in terms of " minimum completely inhibiting concentration " of antibiotic, into sensitive, intermediate, and resistant. Of the strains tested, 25% were sensitive to penicillin, 2% intermediate, and the rest resistant; 66% were sensitive to aureomycin and 33% resistant; the majority, however, were intermediate in their sensitivity to chloramphenicol.

Ability of the strains to produce penicillinase exhibited a striking relation to their susceptibility to penicillin. To determine the effect of resistance resulting from exposure to penicillin *in vitro*, 12 initially highly sensitive strains of staphylococci were transferred daily by serial subculture on to agar plates containing increasing concentrations of the antibiotic. It was found that after 25 such transfers the organisms were able to withstand 100 μg. or more per ml., none of them at any time producing penicillinase. Furthermore, these micro-organisms did not lose their coagulase-producing ability, which is in contrast to what occurred with erythromycin and magnamycin, when some of the adaptively resistant strains lost this property.

No direct correlation was found between degree of sensitivity to any of the antibiotics and the source of the staphylococci. No penicillin-resistant strain was resistant to aureomycin or oxytetracycline, but all strains resistant to these two antibiotics were resistant to penicillin. On the other hand, the majority of penicillin-resistant strains were sensitive to aureomycin or oxytetracycline. There was some suggestion either that staphylococcal strains were naturally resistant to one or more antibiotics, or that they acquired resistance by exposure in other hosts and were then obtained by contact or general dissemination. *Malcolm Woodbine*

947. **Pathogenesis of *Candida albicans* Infection Following Antibiotic Therapy. I. The Effect of Antibiotics on the Growth of *Candida albicans***
M. HUPPERT, D. A. MACPHERSON, and J. CAZIN. *Journal of Bacteriology* [*J. Bact.*] **65**, 171–176, Feb., 1953. 2 figs., 22 refs.

Many micro-organisms might be described as " opportunists ", in particular most Gram-negative bacteria and the yeast-like fungus *Candida albicans*. The recent increase in " candidiasis " as a complication of antibiotic therapy has been attributed variously to: (1) what has been called " suppression with substitution " (that is, the killing off of susceptible organisms, thus allowing a vast increase in the number of resistant organisms); (2) to a disturbance of the normal flora leading to nutritional imbalance so as to affect the integrity of the mucous membranes of the host and thus give an entry to organisms normally unable to penetrate healthy mucosa; or (3) to a direct stimulation of the growth or virulence of *C. albicans* by the antibiotics. In this contributory study the authors, working at the University of North Carolina School of Medicine, made quantitative measurements of the effect of antibiotics on *C. albicans in vitro*.

Four stock cultures of *C. albicans*, maintained on Sabouraud glucose agar, were continuously incubated at 37° C. and transferred once weekly to a semi-synthetic broth of *p*H 6·0. For all cell counts, turbidity measurements, and nitrogen determinations the growth was separated by centrifugation, washed in normal saline, and adjusted to *p*H 6·0 with hydrochloric acid. A micro-Kjeldahl method was used for the nitrogen determination, which preliminary experiments had shown to be the most reliable index of cellular growth. The highest concentration of antibiotics employed was approximately 100 times the maximum level commonly attained in blood. All the cultures were incubated at 37° C. for 48 hours, boiled in a water bath for 15 minutes, and separated, washed, and transferred to 50-ml. volumetric flasks, from which aliquots were taken for nitrogen estimations.

The results showed that in 21 control estimations without antibiotics an average of 1·01 mg. of nitrogen per ml. was obtained; similar results were obtained in the presence of penicillin, chloramphenicol, terramycin (oxytetracycline), and streptomycin, showing that these four antibiotics had no stimulatory or inhibitory effect. Aureomycin, however, at more than 0·1 mg. per ml., clearly increased the total growth of all 4 strains of *C. albicans*, and nearly identical results were obtained with three different preparations of aureomycin. These results are discussed in relation to those obtained by other workers. *Malcolm Woodbine*

948. **The Sensitivity to Antibiotics of Strains of *Bact. coli* Associated with Infantile Gastro-enteritis**
J. SMITH and W. H. GALLOWAY. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **28**, 30–35, Feb., 1953. 26 refs.

At the City Hospital, Aberdeen, the authors tested the bacteriostatic and bactericidal action of terramycin hydrochloride (oxytetracycline), chloramphenicol, aureomycin hydrochloride, and dihydrostreptomycin on 24 strains, each of 3 types, of *Bacterium coli*, O111 B4 H2, O111 B4 H12, and O55 B5 H6, the organisms suspected of causing infantile gastro-enteritis. One drop of a 1-in-10 dilution of a 24-hour broth culture of each strain was added to 1 ml. of broth in tubes containing concentrations of the antibiotics decreasing from 50 to 1·5 μg. per ml. Cultures were inspected after 24 and 48 hours' incubation at 37° C., and those without visible growth were plated. Oxytetracycline had the most powerful inhibitory action, followed by chloramphenicol and then aureomycin; bactericidal action by these three antibiotics was observed on only a few strains, and then only after 48 hours and in the higher concentrations. Dihydrostreptomycin was the least inhibitory but the most bactericidal.

Of 140 infants excreting *Bact. coli* O55 B5 H6 in the faeces on admission to hospital, 107 were given a 6-day

course with one of the drugs listed below, and 33 remained untreated and acted as a control group. A comparison was then made in the 8 groups of the average number of days from time of admission to disappearance of the organism from the faeces. The over-all results are shown in the following table:

Treatment	Dose	No. of Patients	Days Infective
None (control group)	—	33	16
Sulphadimidine ..	0·5 g., then 0·25 g. 4-hourly	9	13
Penicillin	50,000 units, then 25,000 units 4-hourly ..	8	19
Polymyxin	50 mg. 6-hourly.. ..	17	12
Dihydrostreptomycin	20 mg. per kg. body weight 6-hourly ..	15	16
Aureomycin ..	10 mg. per kg. 6-hourly	7	12
Chloramphenicol ..	50 mg. per kg. 6-hourly	35	14
Oxytetracycline (terramycin)	50 mg. per kg. 6-hourly	16	16

In a similar investigation on 29 infants infected with *Bact. coli* O111 B4 H2 it was again found that disappearance of the organism from the faeces occurred in about the same time in the controls as in treated cases. It was found, however, that during the period of administration of the drugs the growth of the intestinal flora, and particularly of the specific types discussed, was markedly suppressed, and the authors consider that this is bound to limit the possible spread of cross-infection. Drug resistance of the strains was not studied.

In a further study of 21 infants in a residential nursery, *Bact. coli* O55 B5 H6 was isolated from the faeces of 15 patients, of whom 3 had moderate diarrhoea and were sent to hospital, 7 had mild diarrhoea, and 5 were symptom-free. The 18 infants retained in the nursery were given a 6-day course of oxytetracycline (100 mg. 4 times daily by mouth). Two days later 1 infant, and 8 days later 7 infants, were still excreting the organism. After further courses of the antibiotic the 2 infants whose faeces were still positive (1 in pure culture) were treated in hospital and became negative. In none of the 6 cases with negative stools at the start did they become positive. *Joyce Wright*

949. **Dosage of Antibiotics. Relation between the *in-vitro* and *in-vivo* Concentrations Effective in Urinary-tract Infections**

J. C. Gould, J. H. Bowie, and J. D. S. Cameron. *Lancet* [*Lancet*] **1**, 361–364, Feb. 21, 1953. 8 refs.

At the Royal Infirmary, Edinburgh, 17 patients with urinary-tract infections were given various antibiotics in doses calculated to produce the same concentration in the urine as was known to inhibit the infecting organism *in vitro*. This calculated dose was often much smaller than the standard dose, but the results obtained were as good clinically and pathologically as those achieved with the standard dose. Further advantages were a reduction of toxic side-effects and in the number of resistant organisms encountered. No case of drug resistance was observed during the first course of treatment, though all the bacteria isolated were capable of becoming resistant *in vitro*, and 3 became resistant *in vivo* on standard dosage. [It is particularly impressive that 9 of the patients were given streptomycin, in some cases for 5 days or more.]

The antibiotic was administered 6-hourly, the dose being calculated by multiplying the sensitivity of the organism, expressed in μg. per ml., by the average 6-hourly volume of urine, and multiplying the product by the reciprocal of the 6-hourly excretion rate of the antibiotic (to allow for the proportion not excreted in the urine). The final value was multiplied by a dose-enhancing factor which varied from 1 to 15 and covered the known variation in excretion of individual antibiotics. In preliminary experiments on a group of students and patients with a healthy urinary tract the mean 6-hourly urinary excretion of the various antibiotics after one dose was: penicillin 80%, streptomycin 20%, chloramphenicol 3·4%, aureomycin 27%, and terramycin (oxytetra-cycline 7·5%. *Peter Story*

950. **Laboratory Studies on " Ilotycin "**

H. M. Powell, W. S. Boniece, R. C. Pittenger, R. L. Stone, and C. G. Culbertson. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **3**, 165–182, Feb., 1953. 6 refs.

The authors have further studied, at the Lilly Research Laboratories, Indianapolis, the antibiotic erythromycin (" ilotycin ") recently isolated from *Streptomyces erythreus* by McGuire *et al.* (*Antibiot. and Chemother.*, 1952, **2**, 281; *Abstracts of World Medicine*, 1953, **13**, 13). This drug possesses significant activity *in vitro* against many Gram-positive organisms and some members of the *Brucella*, *Haemophilus*, and *Neisseria* groups.

In the present investigation tests on mice have shown that erythromycin possesses marked protective action against infections due to haemolytic streptococci and pneumococci, and that it also has demonstrable inhibitory activity against mouse infections with the viruses of meningo-pneumonitis and lymphogranuloma venereum when these are given intranasally. No activity was demonstrable against smaller viruses, including MM, Semliki Forest, rabies, poliomyelitis, and influenza viruses. *A. W. H. Foxell*

951. **Mode of Action of Streptomycin in Relation to the Changes in Spinal Fluid Sugar in Tuberculous Meningitis. I. The Role of Streptomycin as a Reducing Agent and the Specificity of the Shaffer–Hartmann Method for Determining " True Glucose " when this Antibiotic is Used (*in vitro* Experiments)**

R. H. Friedman and A. F. Hartmann. *Journal of Pediatrics* [*J. Pediat.*] **42**, 157–160, Feb., 1953. 4 refs.

Streptomycin acts as a reducing agent and may give rise to " false values " for sugar in the cerebrospinal fluid when this is estimated by the Hagedorn–Jensen method. As little as 0·5 mg. of streptomycin per ml. has a " glucose equivalent " of 13·8 mg. per 100 ml. if precipitation of the non-glucose reducing substances is not first effected with copper sulphate and sodium tungstate. When the authors, working at the Children's Hospital, St. Louis, Missouri, made similar estimations by the Shaffer–Hartmann method, with addition of 5% copper sulphate and 6% sodium tungstate to precipiate non-glucose

reducing substances from solution, true glucose determinations were found not to be invalidated when concentrations of streptomycin were within the physiological range. *A. W. H. Foxell*

952. **"Continuous" *vs.* "Discontinuous" Therapy with Penicillin. The Effect of the Interval between Injections on Therapeutic Efficacy**
H. EAGLE, R. FLEISCHMAN, and M. LEVY. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 481–488, March 19, 1953. 1 fig., 12 refs.

The relative efficacy of continuous and discontinuous administration of aqueous sodium benzylpenicillin to mice with an infection due to group-A streptococci was investigated at the National Institutes of Health, Bethesda, Maryland.

The authors found that "cure was effected most rapidly by the continuous provision of maximally effective concentrations of the drug. If penicillin was given so infrequently that the concentration at the focus of infection fell to ineffective levels in the interval between injections, the time necessary for cure was correspondingly increased. . . . In the interval between injections the host contributed slightly but definitely to the result". Small doses, repeated often enough to maintain an effective level at the focus of infection, achieved a cure just as rapidly as massive doses similarly administered.

It is pointed out that the maximum effective concentration of penicillin in the blood is usually three to ten times the "inhibitory" concentration as determined by sensitivity tests, and since half the circulating penicillin is bound to the serum protein, the serum concentration should be five to twenty times the "inhibitory" level for the organism.

Examples are given of suitable dosage schedules for infections due to a variety of organisms. The authors point out that in arriving at the appropriate schedule the approximate penicillin sensitivity of the organism and the location of the infective process must be considered. *A. W. H. Foxell*

953. **Absorption following Oral Administration of Erythromycin**
J. W. SMITH, R. W. DYKE, and R. S. GRIFFITH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] 151, 805–810, March 7, 1953. 5 figs., 4 refs.

In an investigation carried out at the Indianapolis General Hospital it was found that erythromycin given by mouth to healthy subjects in the fasting state was adequately absorbed, but that after food had been taken little appeared in the blood, the antibiotic being decomposed within a few minutes at *p*H 3 or less. When tablets coated with an acid-resisting material were used, however, absorption was unaffected by food, and the serum level after a single dose of erythromycin was higher than that found in the fasting subject after the ingestion of uncoated tablets.

Thirteen patients with haemolytic streptococcal infections and 7 with pneumococcal pneumonia responded satisfactorily to treatment with 300 to 500 mg. of erythromycin by mouth every 6 to 8 hours. Another patient with pneumonia, who was moribund on admission, failed to respond to treatment although penicillin and streptomycin were also given. Of 11 patients suffering from miscellaneous infections, 8 responded to treatment with erythromycin, the drug having no effect in 2 cases of infection with *Pseudomonas* and one with *Proteus*. One patient with subacute bacterial endocarditis due to *Streptococcus salivarius* responded temporarily, but relapsed.

Of 614 strains of staphylococci tested, two-thirds were inhibited by 0·34 μg. of erythromycin per ml., and no strain required more than 1·56 μg. per ml. Resistant strains developed in 2 cases during treatment, but no serious toxic effects occurred. No effect was noted on the blood count, plasma protein and serum bilirubin levels, cephalin flocculation and thymol turbidity reactions, bromsulphalein excretion, or blood urea, nitrogen, and prothrombin levels. Four of 6 patients tested showed slight reduction of clotting time while they were receiving the drug. *Robert Hodgkinson*

954. **Terramycin by Subcutaneous Clysis**
W. J. FARLEY and L. KONIECZNY. *Journal of Pediatrics* [*J. Pediat.*] **42**, 177–184, Feb., 1953. 1 fig., 12 refs.

The authors, in an investigation at St. Michael's Hospital, Newark, New Jersey, have given oxytetracycline (terramycin) by hypodermoclysis in the treatment of a variety of infections—including bronchopneumonia, bronchiolitis, otitis media, and enteritis—in infants and children. For this purpose they used the antibiotic in the form of the hydrochloride buffered with the sodium salt of glycine to give a relatively stable solution with a *p*H of about 9. This was employed 254 times in the treatment of 36 children, the majority of whom were also given oxytetracycline or other antibiotics orally at the same time.

The results are stated to have been satisfactory in all but 2 of these 36 cases. One hour after a single dose of 10 mg. per kg. body weight in 4 cases the serum concentration of oxytetracycline was 2·5 to 5·0 μg. per ml., and at 12 hours was 0·625 to 1·25 μg. per ml. In 2 patients without apparent meningeal inflammation no trace of the antibiotic could be detected in the cerebrospinal fluid in spite of a high level in the serum.

A dose of 10 mg. oxytetracycline per kg. body weight in a concentration of 1 mg. per ml. every 12 hours is recommended for routine use. In the treatment of severe infections it is suggested that doses of 20 to 25 mg. per kg. body weight may be necessary, but that the concentration should not exceed 5·0 mg. per ml. The antibiotic, which appears to be compatible with hyaluronidase, may be added to physiological saline, dilute dextrose solution, 1/6 M sodium lactate, or Darrow's solution. Protein hydrolysate and Ringer's solution were not used in the trial reported as it was noted that a fine precipitate or a turbid solution sometimes formed on addition of oxytetracycline.

The authors believe that the administration of this wide-range antibiotic by hypodermoclysis is a useful mode of therapy in the management of infectious disease in childhood, especially when other methods of administration are impracticable. *A. W. H. Foxell*

Infectious Diseases

955. **Poliomyelitis Virus in Human Blood during the "Minor Illness" and the Asymptomatic Infection**
D. M. HORSTMANN and R. W. MCCOLLUM. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **82**, 434–437, March, 1953. 1 fig., 15 refs.

A stage of viraemia is known to precede the appearance of the clinical signs of involvement of the central nervous system in experimental poliomyelitis in chimpanzees and cynomolgus monkeys. In this report from Yale University School of Medicine evidence is presented indicating that a similar state of viraemia occurs in human subjects infected with the poliomyelitis virus.

During an epidemic of poliomyelitis in a small town in Ohio in 1952, throat and rectal swabs and blood samples were taken from contacts and from children with any mild febrile illness possibly attributable to the earliest stage of infection with the poliomyelitis virus. Tissue cultures and rhesus monkeys were used for testing blood specimens, while tissue culture alone was employed for the testing of throat and rectal swabs. In one family of 4 children, none of whom had been in contact with a known case of the disease, the 3 eldest developed a mild febrile constitutional upset, and the youngest, aged 2, remained well. None subsequently developed poliomyelitis, yet the virus of the disease was isolated from the blood and from throat and rectal swabs of all 4 children. In these children, therefore, as may occur in experimental infections in monkeys. the presence of poliomyelitis virus in the blood was not associated with clinical signs of involvement of the central nervous system. This state of viraemia probably occurs soon after ingestion of the virus, and gives rise in some, but not all, cases to slight fever, anorexia, nausea and vomiting, headache, and sore throat, paralysis not developing until a week or so later, if at all.

D. Geraint James

956. **ACTH in Reiter's Syndrome. Four Cases, with Review of the Literature**
E. LARSON and S. J. ZOECKLER. *American Journal of Medicine* [*Amer. J. Med.*] **14**, 307–317, March, 1953. 5 figs., 33 refs.

To the 3 cases of Reiter's syndrome treated with ACTH already reported in the literature the authors add 4 more which were seen at the Veterans Administration Hospital, Des Moines, Iowa.

The first patient, a man of 24, had a severe attack of Reiter's syndrome which did not respond to administration of salicylates, penicillin, streptomycin, or a non-specific protein; he resisted physiotherapy because of pain and stiffness in the joints. After a course of ACTH in doses of 25 mg. every 6 hours the patient was able to walk, his appetite and general condition improved, and physiotherapy could be carried out satisfactorily. Hospital treatment in this case lasted 7 months. The second patient had an even more severe attack of Reiter's syndrome, which required 15 months' hospital treatment. The authors believe that had it not been for the administration of ACTH physiotherapy in this case would have been impossible and the residual deformity would have been severe. The third patient, who had the most severe attack of Reiter's syndrome, became refractory to ACTH, and marked osteoporosis developed. Physiotherapy, although painful, was persisted in, as was administration of ACTH, and the patient recovered completely, the duration of treatment having been 17 months. The fourth patient, who had a less severe attack than the others, had had a short course of cortisone, with temporary relief of symptoms, before admission to hospital. Arthritis recurred and he was admitted to hospital, where administration of ACTH permitted physiotherapy to be maintained until all joint distress had disappeared.

The authors conclude that ACTH has a definite place in the over-all management of Reiter's syndrome.

James D. P. Graham

See also Pathology, Abstract 910.

957. **Experimental Studies on Sarcoidosis. Persistence and Survival of Inoculated Micro-organisms**
A. ROSTENBERG, F. J. SZYMANSKI, G. J. BREBIS, J. B. HAEBERLIN, and F. E. SENEAR. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **67**, 306–314, March, 1953. 2 figs., 8 refs.

Inoculations were made with living B.C.G. organisms and living *Mycobacterium smegmatis* or *Bacillus subtilis* into 13 patients with sarcoidosis and 11 patients with diseases other than sarcoidosis. No differences were noted between the patients with and those without sarcoidosis with regard to (1) the gross or pathologic alterations induced by the inoculations of the organisms, (2) recovery of the inoculated organisms, and (3) the change of cutaneous tuberculin sensitivity as a consequence of the B.C.G. inoculation.

It is concluded that the theory of positive anergy is erroneous in that it implies that the failure to react is due to some exalted ability to dispose of the antigen or products derived from it. We do not assert that the failure of patients with sarcoidosis to react to tuberculin is on the same basis as that of the person who was never exposed. We do assert that the failure of people with sarcoidosis to convert from tuberculin negativity to positivity when inoculated with B.C.G. is not due to the fact that they have any immunity toward the tubercle bacillus but is due to other, as yet unknown, reasons.

It is concluded that the tuberculous etiology of sarcoidosis is very unlikely.—[Authors' summary.]

Tuberculosis

958. **Tuberculosis in Medical Students, Dental Students and Nurses. A Five Year Study, 1945–50, at Guy's Hospital**

A. BATTY SHAW. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **102**, 36–55, 1953. 3 figs., 11 refs.

The author reports his findings in a study of tuberculosis among 920 nurses and 1,113 medical and dental students at Guy's Hospital, London, during the period 1945–50. While the percentage of positive reactors among the medical students and nurses did not show any great difference from that found in the Prophit Survey in 1937–43, in the more recent survey the tuberculin conversion rate of both students and nurses was found to be considerably lower. The Prophit Survey showed that 75·5% of the medical students and 72·2% of the nurses had converted after 3 years: the figures in the present investigation were 48·4% for medical students and 45·7% for nurses.

The study also showed that the incidence and morbidity rate of tuberculosis among the students and nurses in the recent survey was lower than in that of 1937–43, the figures (expressed as the annual rate per 1,000 observation years) being 2·6 for male students and 4·4 for nurses in 1945–50, as compared with 5·1 and 8·9 respectively for the period 1937–43. Both results—the fall in the tuberculin conversion rate and in the morbidity rate during the period 1945–50—point to a definite improvement in the control of tuberculosis, and to the value of the precautionary measures, such as tuberculin testing and chest radiography, which have been carried out at the hospital. In view of the higher morbidity rate among nurses showing negative tuberculin reactions the author considers that vaccination with B.C.G. is justified, should the results which have been claimed for this vaccine be confirmed in Great Britain. *Franz Heimann*

959. **The Double Epidemiology of Tuberculosis in Scotland and the Netherlands.** [In English]

M. STRAUB. *Documenta de medicina geographica et tropica* [*Docum. Med. geogr. trop. (Amst.)*] **5**, 85–92, March, 1953. 2 figs., 12 refs.

In this excellent paper from the Pathological Laboratory of the Municipal Hospitals, Rotterdam, the relation of primary enterogenous and primary pulmonary infection to death rates from tuberculosis in Scotland and in the Netherlands is compared. Some 75 years ago the proportion of enterogenous to pulmonary primary infection in Amsterdam was 1 to 5. This proportion increased until, in 1937, it was almost 1 to 1, and 30% of individuals in the age group 10–20 had an enterogenous primary focus. Although pulmonary infection had diminished, there had been an absolute increase in bovine infection, probably due to the pooling of milk from many different sources. During this time, however, when bovine infection was most common, bovine bacilli were found in only 10% of cases of tuberculosis. Since the human and bovine organisms are equally virulent to man, it is the portal of entry, and therefore the site of the primary focus, which renders enterogenous infection less dangerous than a pulmonary primary focus, the lung being much more susceptible to the bacillus.

In Scotland in 1926 enterogenous far exceeded pulmonary primary infection, but since 1930, when measures against bovine tuberculosis began, there has been a marked decline in deaths from intestinal and peritoneal tuberculosis. It is notable, however, that during the same period the death rate from pulmonary tuberculosis and extrapulmonary tuberculosis increased, and it is probable that this was not entirely due to the war. Since 1940 the death rate from tuberculous meningitis has risen from 42% to 57% of the total mortality from extrapulmonary tuberculosis. The increase in mortality in Scotland in young adults is, in the author's view, a result of the lessened " natural bovine vaccination " due to the diminution of mesenteric primary infections since the campaign against bovine tuberculosis began. This is borne out by Pitcher who stated (*Lancet*, 1951, **2**, 786) that in countries where 75% of the cows are attested as being free from tuberculosis the number of notifications of pulmonary tuberculosis rose, whereas in countries where the attested cattle did not exceed 15% of the total the notified cases decreased in the same period.

In the Netherlands, since the decline in bovine infection, an increase in morbidity from infections due to the human strain has not been observed. The author considers that this is because in Scotland the morbidity from tuberculosis is much higher than in the Netherlands, and there is probably much more tuberculosis following directly from the primary lesion. In Holland pulmonary tuberculosis is mainly due to re-infection, and resistance is higher; a change in the average immunity will thus not be shown in mortality figures. An increase in the cases of tuberculous meningitis would, however, be expected, and this has occurred in Rotterdam. In the period 1940–5, 45% of cases of extrapulmonary tuberculosis in that city were cases of meningitis, and in the period 1947–50 this figure had risen to 65%.

T. M. Pollock

960. **The Antithyroid Activity of *para*-Aminosalicylic Acid and of Isoniazid.** (Sull'azione antitiroidea dell'acido *para*-aminosalicilico e dell'idrazide dell'acido *iso*nicotinico)

C. A. BUTARO. *Riforma medica* [*Rif. med.*] **67**, 345–349, March 28, 1953. 26 refs.

Further evidence of the antithyroid action of PAS and isoniazid is provided by the author from the Institute of Clinical Medicine of the University of Perugia. The case is described of a man of 32 suffering from bilateral pulmonary tuberculosis who developed clinical signs of

myxoedema after receiving 1,350 g. of PAS over a period of 6 months. The symptoms receded within 2 months of stopping the treatment. In 6 other patients with pulmonary tuberculosis (3 febrile) and 5 normal subjects there was a slight fall in the basal metabolic rate (B.M.R.) (but within the normal limits of error) after a small single dose of 5 g. of PAS. The effect of isoniazid was investigated in a woman of 36 with the characteristic clinical signs of hyperthyroidism and a B.M.R. of +35%. Experimental administration of 300 mg. of isoniazid daily parenterally caused a definite reduction of thyroid activity, and after 55 g. had been given she showed the characteristic signs and symptoms of hypothyroidism (B.M.R. −45%). On stopping treatment these regressed until an apparently stable condition was reached on a slightly hypothyroid level, with a dry skin and a B.M.R. of −9%.

Later, a series of 10 patients with hyperthyroidism were given 200 to 250 mg. of isoniazid daily for 30 days, with diminution of the clinical symptoms and of the B.M.R., although high B.M.R. readings in neurotic patients were not influenced by isoniazid.

PAS and isoniazid appear to inhibit the synthesis of thyroxine, and the possibility of a corticogenic mechanism in which these drugs act as " stressors " in the sense of Selye is discussed. The antithyroid action of PAS and isoniazid does not seem to have an unfavourable influence on their bacteriostatic effect, and is in any case a rare side-effect which occurs only after prolonged administration.

V. C. Medvei

961. **Experimental Study and Clinical Observations Concerning the Tuberculostatic Action of Isoniazid.** (Étude expérimentale et résultats des observations cliniques concernant l'action tuberculostatique de l'I.N.H.)

C. Gernez-Rieux. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **17**, 48–69, 1953. 5 figs.

This study from Lille of the effect of isoniazid in tuberculosis is divided into two parts, the first consisting of two animal experiments and the second being an investigation of 100 patients with pulmonary tuberculosis who were treated with the drug.

In the first animal experiment 3 groups of guinea-pigs were inoculated with tubercle bacilli. The first group were given 30 mg. of isoniazid per kg. body weight daily, the second 70 mg. per kg., and the third were untreated; treatment was started the day after inoculation, and continued for 32 days. Both doses of isoniazid were strongly bacteriostatic, but in the group receiving the smaller dose generalized lymph-node involvement was evident; in the animals given the larger dose no tuberculous lesions could be found 123 days later. In the second experiment rabbits inoculated intravenously with tubercle bacilli and treated with isoniazid 2 days before inoculation or 2 days or 7 days after inoculation showed no radiographic evidence of pulmonary lesions. In animals treated 14 days or more after inoculation, in all of which there were diffuse pulmonary lesions, considerable regression of the lesions was observed in the radiographs.

In the 100 patients with tuberculosis treatment with isoniazid had been given for periods varying between 2 and 6 months in a daily dose of 4 or 5 mg. per kg. body weight by mouth either alone or combined with streptomycin or PAS. Of these patients 93 had been treated previously with antibiotics without appreciable result. The dosage of isoniazid given produced a plasma concentration of between 1·8 and 2 μg. per ml. after 1½ hours. The highest plasma concentrations were obtained when the drug was given by intramuscular or intravenous injection. A single dose of the drug was eliminated in 24 hours, but at 12 hours appreciable quantities were still present in the blood. In 57% of the cases isoniazid produced a very great clinical improvement, but the removal of the bacillus from the sputum was much more rare. Resistance to the drug was noted in 18 out of 30 cases after 3 months. Toxic effects were uncommon and appeared only when treatment was prolonged.

T. M. Pollock

962. **The Effect of Certain Infectious Diseases on Tuberculin Allergy**

J. W. Bentzon. *Tubercle* [*Tubercle (Lond.)*] **34**, 34–41, Feb., 1953. 4 figs.

All the patients admitted to the Blegdam Fever Hospital, Copenhagen, in the first quarter of 1951 (approximately 500) were subjected to a Mantoux test with 5 T.U. of P.P.D. on admission and again 2 or 3 months later, usually after discharge, the diameter and character of the indurated area being recorded on both occasions. Measles (49 patients), scarlet fever (93 patients), and infectious mononucleosis (46 patients) reduced the diameter and density of the skin response to the second test. The skin sensitivity of patients with measles increased markedly between the first and tenth days after appearance of the rash. Other conditions, such as upper respiratory infections, tonsillitis, pneumonia, gastro-enteritis, and para-dysentery, had no effect on the skin response. Repeated tests on a control group of 35 patients without infectious disease showed no evidence of significant spontaneous variations.

G. G. Meynell

EXTRAPULMONARY TUBERCULOSIS

963. **Use of Pyrazinamide (Aldinamide) in the Treatment of Tuberculous Lymphadenopathy and Draining Sinuses. A Preliminary Report**

J. W. V. Cordice, L. M. Hill, and L. T. Wright. *Journal of the National Medical Association* [*J. nat. med. Ass.*] **45**, 87–98, March, 1953. 10 figs., 11 refs.

The authors report upon the use of pyrazinamide in the treatment of tuberculous lymphadenitis at Harlem Hospital, New York City. Pyrazinamide is pyrazinoic acid amide and is related to nicotinic acid; it has been found to possess antimycobacterial activity.

The drug was given to 19 patients aged between 17 months and 67 years. [For details of dosage the original article should be consulted.] Of these patients, 7 underwent excisional surgery and received the pyrazinamide

at the same time; the others were not operated on, although 3 of them underwent repeated aspiration of abscesses.

The results appear to have been uniformly good. In only one case was there a recurrence, which was brought under control with another course of pyrazinamide. Only one patient suffered from side-effects, in the form of dizziness and gastro-intestinal upset, which cleared as soon as the drug was stopped.

The authors stress that as this is only a preliminary report of the investigation, the follow-up period is necessarily short. *Tom Rowntree*

964. **The Selective Principle in the Treatment of Renal Tuberculosis. Partial Resection of the Tuberculous Kidney**

C. SEMB. *Journal of the Oslo City Hospitals* [*J. Oslo City Hosp.*] **3**, 45–114, March–April, 1953. 15 figs., 22 refs.

This important paper gives a detailed account of the pathology and treatment of urogenital tuberculosis as modified by the introduction of the new drugs, streptomycin, PAS, and isoniazid. Out of a total of 167 cases treated at Ullevål Hospital, Oslo, between December, 1947, and January, 1953, 40 (24%) were treated medically and 40 by unilateral nephrectomy; in the remaining 87 cases (52%), which form the basis of the present study, unilateral or bilateral partial nephrectomy was performed. Both kidneys were involved, with demonstrable lesions, in 21 (25%) of these cases, and in approximately half there were definite lesions of the ureter or bladder; epididymitis was present in approximately one-quarter of the 54 men. Of the 87 patients, 73 (84%) had been treated previously for extra-urogenital lesions.

Pathologically, cases of renal tuberculosis fall into three groups: (1) the parenchymatous form, in which the lesions are confined to the cortex, without gross ulceration; (2) the local destructive form, in which up to two divisions of the kidney (as defined by Löfgren) may have been destroyed by " ulcerocavernous " lesions; and (3) the total destructive form. The diagnosis and classification of the present series were based on routine preoperative pyelography and aortography, findings at operation, and examination of the material removed at operation. In general it was found possible to treat cases in Group 1 with antibiotics alone, while those in Group 3 were treated by standard nephrectomy or nephro-ureterectomy. Thus the majority of cases considered were of Group 2, and a detailed account is given of the distribution of the lesions in these cases.

Ulcerocavernous lesions do not respond to antibiotic treatment alone, but if they are removed by partial nephrectomy, then residual parenchymatous lesions in the remaining portion of the kidney, together with the ureteric and early bladder lesions, respond well to chemotherapy. An account of the author's technique of partial nephrectomy is given, with interesting comments on the maximum length of time the renal pedicle can be clamped without causing permanent damage to the kidney function; it is stated that whereas 40 to 50 minutes of complete ischaemia during partial nephrectomy on a single remaining kidney will give rise to a severe uraemic reaction, intermittent clamping for the same total period interferes much less with renal function. In general, the operation is preceded by 4 to 6 weeks' rest in bed with 10 to 14 g. of PAS daily and a course of streptomycin totalling 8 to 15 g. After the operation PAS is given for a further 4 to 6 weeks in the same dosage, together with 1 g. of streptomycin daily for 1 to 2 weeks and then 1 g. every 3 days to a total of 30 to 40 g.

Of the 87 patients undergoing partial nephrectomy, 39 have been followed up for 2 to 5 years and the remaining 48 for less than 2 years. In approximately 90% of both these groups the disease has been cured, as indicated by disappearance of symptoms and of tubercle bacilli and pus from the urine. In no case has hypertension developed. In 2 cases secondary nephro-ureterectomy had to be performed for stricture of the ureter, but no evidence of spread of the disease has been found and the mortality has been *nil*. The function of the remaining portion of the kidney has been assessed repeatedly by means of intravenous urography and has been found uniformly good in all but 2 cases.

[This paper, by an acknowledged authority on tuberculosis, is profusely illustrated and is outstanding in its detailed and accurate analysis of the material. It introduces a new principle into the treatment of genito-urinary tuberculosis, bringing it into line with the newer treatment of pulmonary tuberculosis, and should be read by all who have to deal with this condition.] *F. B. Cockett*

965. **The Treatment of Paraplegia due to Pott's Disease by Antero-lateral Decompression.** (Traitement des paraplégies pottiques par décompression antéro-latérale)

H. J. SEDDON. *Mémoires de l'Académie de chirurgie* [*Mém. Acad. Chir. (Paris)*] **79**, 281–286, March, 1953. 1 ref.

A persistent paraplegia in Pott's disease may be due to inflammatory products compressing the cord, to mechanical changes in the vertebral column leading to compression by a sequestrum or a necrotic intervertebral disk, or, rarely, to thrombosis of the cord vessels. Paraplegia arising late in the course of the disease is usually due to persistent infection in the spinal canal or to stretching of the cord around a bony prominence.

Intervention may be successful after 6 months of complete paralysis, although after this period its value rapidly diminishes. It is indicated where the paralysis occurs after prolonged confinement to bed, or where it fails to improve on conservative treatment alone. Uncontrollable leg spasms, the advanced age of the patient, or the history of a previous paralysis are grounds for early operation. The surgical procedures normally employed are costotransversectomy and antero-lateral decompression. The former may be sufficient if an abscess under tension is found; if this is not the cause of the paraplegia, the operation can be extended in order to perform decompression. The latter is a more considerable procedure, and carries the risk of increasing the paralysis or of spreading the infection by puncture of the dura or pleura. The operation of laminectomy, except in the cervical region, has been abandoned.

Over a period of 8 years, the author has treated 25 cases, 16 of them successfully: of 10 early paraplegias 7 were cured, and of 15 delayed cases 9 were cured. In early cases early intervention is favoured, since the commonest cause of compression at this stage, namely, abscess or sequestrum, is then easily removed.

Peter Ring

966. **Functional Recovery with Streptomycin in Tuberculosis of the Knee.** (Tentatives de récupération fonctionnelle par la streptomycine dans la tuberculose du genou)
J. P. MEUNIER and J. BÉNARD. *Revue de chirurgie orthopédique* [*Rev. Chir. orthop.*] **39**, 111–119, Jan.–March, 1953.

The authors describe their treatment of 18 cases of synovial tuberculosis of the knee, of which 15 were confirmed by culture or biopsy. Streptomycin was given alone in doses of 1·5 g. per day for 120 days, followed in 10 cases by a further course of 1 g. per day. The limb was immobilized for 2 months, and at the end of this period, if resolution appeared to be proceeding, active movements were started. Walking was allowed after a further 2 months, that is, usually 4 months from the beginning of treatment.

The immediate results in 15 patients were good, normal activities were resumed without pain, and range of movement varied from full extension to a flexion range between 120 degrees and 60 degrees. The results were poor in one patient with associated pulmonary tuberculosis, in a second patient who appeared on examination to have a fair result but could only walk with the knee extended, and in a third with a good initial result but who subsequently sustained a supracondylar fracture of the knee which led to limitation of movement.

Peter Ring

967. **A Comparative Study of the Effect of Combined Treatment with Streptomycin and Isoniazid on the Course of Tuberculous Meningitis.** (Primi rilievi differenziali nel decorso della meningite tubercolare trattata con streptomicina associata ad idrazide isonicotinica (I.A.I.))
F. RAGAZZINI, M. GIUSTI, and R. COCCHI. *Rivista di clinica pediatrica* [*Riv. Clin. pediat.*] **51**, 110–122, Feb., 1953. 6 figs., 7 refs.

The authors compare the results, in the treatment of 111 cases of tuberculous meningitis at the Paediatric Clinic, University of Florence, of various different combinations of therapy. At first they gave streptomycin, alone or with PAS and sulphone (21 cases), then streptomycin as a first course, followed by streptomycin and isoniazid (30 cases), and most recently they have employed a combination of streptomycin and isoniazid throughout (60 cases). They describe the variations in the protein content of the cerebrospinal fluid, and compare the time required in the three groups of cases for the fluid to return to normal.

Whereas in the first two forms of treatment the protein level tended to rise during the first month and showed little sign of decreasing until after the third month, with streptomycin and isoniazid the fall was more rapid, being well marked by the second month. In 17 cases from each group the times taken for the cisternal fluid to become normal are compared. In the period when streptomycin alone or in combination with PAS was used the average time was 7 months, with a minimum of 3 months (in one case) and a maximum of 11 months. In the third period, when streptomycin and isoniazid were given, the average time was 3·5 months, with a minimum of 2 months (in 4 cases) and a maximum of 6 months (in one case). In the second period the times were intermediate [as might be expected].

Reviewing their total of 111 cases, excluding patients who died during the first week of treatment, the authors find a considerable improvement in results. The mortality has fallen from 12% to 5%, and the percentage of cures, based on examination of the cerebrospinal fluid, has risen from 4·8% to 30%. The authors are well aware that these figures are not final, but taking into account also the general improvement in the cases at present under treatment, they feel that the combination of streptomycin and isoniazid is a great advance in therapy in these cases. [The results are well presented in a number of useful graphs.] *J. G. Jamieson*

PULMONARY TUBERCULOSIS

968. **Infiltration along the Line of the Pulmonary Fissure in Advanced Tuberculosis and its Pathological Significance.** (Infiltrats en bande juxta-scissuraux au cours de la phtisie tertiaire et leur signification pathologique)
J. BRUN and L. F. PERRIN. *Poumon* [*Poumon*] **8**, 809–819, Dec., 1952. 6 figs., 19 refs.

The authors describe the radiological, anatomical, pathological, and therapeutic aspects of a lesion occasionally seen in advanced tuberculosis, presenting radiologically as a narrow band of homogeneous opacity in the immediate neighbourhood of a pulmonary fissure and varying in extent. In the anterior view the opacity may occupy all or a part of the lung field. At the superior border of this opacity, either in direct association or with healthy tissue intervening, are visible one or more advanced tuberculous lesions. In the right lung its most common position is in the posterior and axillary segments of the upper lobe. Seen laterally, the appearance is triangular, with the apex at the junction of the fissures and the base merging with the posterior thoracic wall; in some cases these limits are exceeded. In the left lung the opacity is more elongated and follows the line of the interlobar fissure. An anterior view shows a shadowing extending over almost half the lung field. Laterally the shadow appears as a narrow band running from top to bottom of the field. There are other less characteristic forms.

Thoracoscopic examination, with a view to the possibility of obtaining satisfactory collapse by pneumothorax in these cases, has shown that these opacities are by no means mainly pleural in origin. They appear to be produced by numerous atelectatic areas caused by dissemination from the lesions above. In support of this

view is the fact that the fissure in some cases is convex. Examination by thoracoscopy also suggests the parenchymal nature of these lesions. The appearances described are not common, the authors having seen only 14 typical cases. Of these, 13 were treated by collapse therapy and one with antibiotics. The most important aim in treatment is to obtain healing of the cavities giving rise to dissemination. *T. M. Pollock*

969. **Collapse Therapy for Tuberculous Psychotic Patients**
G. N. J. Sommer, A. M. Balter, H. S. Hatch, and H. J. Muendel. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 232–246, Feb., 1953. 6 refs.

In this paper the authors present their results since 1946 in the treatment of pulmonary tuberculosis in psychotic patients in two mental hospitals in New Jersey. The number of patients was too small to make a statistical summary of any value, but the following facts emerged. Rest in bed and sanatorium treatment are of value. Minor collapse procedures, such as phrenic crush, artificial pneumothorax, or artificial pneumoperitoneum appear to have a very limited field of usefulness. The best results were obtained with thoracoplasty, and in a few cases resection also gave good results.

[This article is interesting, and illustrates how much can be done to control pulmonary tuberculosis in mental hospitals by the use of collapse therapy.]

R. H. J. Fanthorpe

970. **Tuberculous Tracheo-bronchitis. A Study of the Relationship between Bronchoscopic Appearances, Histological Findings and the Complications of Lung Resection**
L. E. Houghton and F. E. Joules. *Tubercle* [*Tubercle* (*Lond.*)] **34**, 74–80, March, 1953.

An investigation was carried out for the British Tuberculosis Association to ascertain the incidence of tuberculous tracheo-bronchitis in patients suffering from pulmonary tuberculosis at a number of hospitals in and near London.

In the first part of the investigation bronchoscopy was performed on a total of 386 patients at 6 different hospitals, the patients being unselected except that they represented every fifth admission to hospital during the years 1950 and 1951. The bronchoscopic appearances were regarded as abnormal in 131 of the 386 patients, there being gross mucosal changes—oedema, granulations, or ulcerations—in 59, stenosis or distortion in 22, and minor mucosal changes in 50. The age and sex of the patient and the duration of disease did not appear to be significant factors in the incidence of bronchial abnormalities. In only 48 out of the 131 cases were there clinical signs indicative of endobronchial disease, while similar clinical findings were noted in 36 of the 255 patients in whom the bronchoscopic appearances were normal. In no case was there any radiological evidence of spread of the disease as a result of bronchoscopy, and only in 3 cases was there a transient rise in temperature.

There was a wide variation, as between the 6 different hospitals, in the percentage of cases in which the bronchoscopic appearances were considered to be abnormal—from 18 to 85%; this the authors attribute to the absence of agreement as to what constitutes the normal.

In the second part of the investigation bronchoscopy was carried out on 95 patients shortly before resection was performed, the findings being studied along with those of histological and bacteriological examination of portions of the bronchus from the point of section. In 39 cases the bronchoscopic appearances were considered to be abnormal, and in 37 of these there was histological evidence of disease, the changes being regarded as severe in 27. Of the 56 cases in which the bronchoscopic appearances were normal, histological evidence of disease was found in 53, the degree of disease being severe in 32 of them. There were 4 deaths in the group of 56 patients and 5 in the group of 39. The incidence of post-operative fistula and empyema appeared to increase with the severity of the disease as found histologically.

D. Weitzman

971. **Short-term Postural Reduction as a Prelude to Active Treatment**
J. P. Lyons. *Tubercle* [*Tubercle* (*Lond.*)] **34**, 87–95, March, 1953. 3 figs., 3 refs.

Postural retention for 2 to 12 weeks, as a short-term therapeutic measure preceding collapse therapy, has been practised at the Grosvenor Sanatorium, Ashford, Kent, since 1948, and the results obtained in 62 cases are described in the present paper. In 44 cases substantial reduction in the size of the cavity was observed, this being apparent in 30 of the cases within 6 weeks. It was found that the larger the cavity, especially if it was of recent origin and thin-walled, the more likely it was to respond to posture; cavities in the dorsal lobe responded particularly well. After this initial period of postural treatment, which was combined with chemotherapy in 15 of the cases, collapse therapy was instituted. In 43 of the 62 patients the disease was arrested, the patient being symptom-free, the sputum being negative, and there being no evidence of cavitation on a plain radiograph at the time of discharge from hospital. Two illustrative cases are described in detail.

D. Weitzman

972. **The Circumstances Leading to Tuberculous Cavitation of the Middle and Lower Parts of the Lungs.** (Circonstances d'apparition des cavernes tuberculeuses des régions moyennes et inférieures des poumons)
A. Dufourt, J. Brun, and A. Dépierre. *Poumon* [*Poumon*] **9**, 95–115, Feb., 1953. 9 figs., 15 refs.

The authors describe the circumstances leading to the formation of tuberculous cavities in the middle and lower regions of the lungs, that is, in the lower and middle lobe on the right side and the lower lobe and lingula on the left. They divide the lesions into "primo-secondary" cavities and "tertiary" cavities, corresponding to the stages of the primary disease. Primary cavities are rare in the early stages, occurring only about once in every 100 primary infections, but later may be found as often as once in 7 cases. They arise from ulceration of the primary focus, whereas true secondary cavities are due to ulceration of foci of bronchopneumonia which have resulted from perforation of primarily infected bronchial

nodes; secondary-stage cavities occur predominantly in the middle lobe of the right lung.

Tertiary cavities occur alone in the absence of lesions in the upper zone in only about 3% of cases, and are predominantly in the apical segment of the lower lobe. They may arise from: (1) an Assmann's focus, though this is rare; (2) pneumonia; (3) ulceration of a tuberculoma; and (4) fairly frequently, by reactivation of a primary calcified lesion. Most commonly tertiary cavities are associated with lesions in the upper zone and are considered to be secondary to the upper-zone lesion, as a result of bronchogenic spread. The authors stress the importance of treating the cavity in the upper zone efficiently even if it appears smaller than the cavity in the lower region. In conclusion they stress the frequency (20%) of cavities occurring in the region of a primary focus, either immediately or even many years after the primary infection, and also emphasize the large percentage (33%) of " daughter " cavities which remain patent unless the original cavity in the upper zone is treated.

G. M. Little

973. **The Effect of Streptomycin Therapy on the Bronchocavitary Junction and its Relation to Cavity Healing**

O. AUERBACH, H. L. KATZ, and M. J. SMALL. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 173–200, Feb., 1953. 8 figs., 30 refs.

A special study has been made at the Veterans Administration Hospitals, Staten Island and Brooklyn, New York, of the process of cavity closure in cases of pulmonary tuberculosis treated with streptomycin. Although only 8 cases were included in the investigation, the findings were so frequent and consistent that the authors consider a report to be justified.

Briefly their conclusions are as follows. When streptomycin is given in the treatment of tuberculous cavities some re-epithelization of the bronchus at the broncho-cavitary junction occurs and the lumen of the bronchus remains patent. In patients not treated with streptomycin there is permanent obliteration of the bronchus at the broncho-cavitary junction. Epithelization at the broncho-cavitary junction prevents obliteration of the bronchial lumen at this site; this is an important factor in preventing permanent closure of the corresponding cavity. The lumen of such cavities is greatly diminished in size and the contents become inspissated, with deposition of calcium within the necrotic centre.

Kenneth Marsh

974. **Isoniazid in the Treatment of Exudative Pleurisy.** (L'isonicotinilidrazide nella pleurite essudativa)

G. RICCI and L. RAVAZZONI. *Minerva medica* [*Minerva med.* (*Torino*)] **44**, 735–738, March 21, 1953. 6 refs.

Details are given of the clinical findings and progress in 6 cases of primary pleural effusion treated with isoniazid at the University Paediatric Clinic, Rome. The diagnosis was confirmed by pleural puncture, and isoniazid was given in doses of 300 mg. daily by mouth; in 3 cases 50 to 100 mg. was also given intrapleurally daily for 3 to 8 days. In every case there was satisfactory resolution of fluid, fall of temperature, and return of the erythrocyte sedimentation rate to normal levels in 2 to 3 weeks.

The authors concede that this condition tends to run a similarly benign course even in the absence of treatment, but they feel that isoniazid confers some benefit, in particular in hastening the reabsorption of the fluid.

D. Weitzman

975. **A Contribution to the Study of Isoniazid Treatment in Tuberculosis.** (Contributo allo studio della terapia antitubercolare con idrazide dell'acido isonicotinico)

G. ASTALDI, P. GORINI, and G. GALDI. *Minerva medica* [*Minerva med.* (*Torino*)] **44**, 738–744, March 21, 1953. 9 figs., 22 refs.

From the University Clinic, Pavia, the authors report their experience with 28 cases of pulmonary tuberculosis which they treated with 300 mg. of isoniazid daily for periods of 7 to 24 weeks. In 19 of the patients the disease was of the exudative type and of recent onset.

In the acute cases, diminution of toxaemia, general improvement, and weight gain were striking, and tended to precede radiological evidence of resolution of the lung lesions. The fall in erythrocyte sedimentation rate did not always parallel these other manifestations of improvement. In 9 cases the sputum became negative for tubercle bacilli, and in others the number of bacilli diminished. In 13 cases, including 10 acute cases, there was complete radiological resolution of the pulmonary lesions, and in 9 others partial resolution was observed. These changes were sometimes apparent after only 6 weeks of treatment. In 4 cases with cavitation, however, there was little improvement.

Liver function tests showed evidence that the drug exerts a toxic effect on the liver, but the authors claim that the administration of " hepatoprotective " substances, such as glucose, vitamin B_{12}, and ascorbic acid, is followed by reversion of the liver function to normal.

D. Weitzman

976. **The Sensitivity to Isoniazid of Tubercle Bacilli Isolated from the Sputum of 29 Patients before and during Treatment.** (Sensibilité à l'hydrazide de l'acide isonicotinique des bacilles de Koch isolés de l'expectoration de 29 malades avant et pendant traitement)

J. LETACON, P. DUBREUIL, J. POULET, and J. FOURCHON. *Presse médicale* [*Presse méd.*] **61**, 324–325, March 7, 1953. 7 refs.

Sputum was examined on 3 occasions from 29 patients suffering from chronic pulmonary tuberculosis, 5 of whom had received isoniazid for at least 2 months before the first sputum test, and all of whom received it up to the time of the last test, 3 months later, together with PAS or streptomycin in 18 cases. No increase in the resistance of the tubercle bacilli isolated from the sputum to isoniazid was found on any occasion. The minimum inhibitory concentrations were between 0·06 and 1·0 μg. per ml., less than the concentration reached in the plasma during treatment (0·6 to 3·0 μg. per ml.).

G. G. Meynell

Venereal Diseases

977. **Production of Immobilizing Antibodies Unaccompanied by Active Immunity to *Treponema pallidum* as Shown by Injecting Rabbits and Mice with the Killed Organisms**

C. P. McLeod and H. J. Magnuson. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 9–22, Jan., 1953. 15 refs.

A study was carried out at the U.S. School of Public Health, Chapel Hill, North Carolina, of the immunological response of rabbits and mice to killed inocula of the Nichols strain of *Treponema pallidum*. The results confirmed the findings of other investigators that the presence of reagin does not confer immunity in rabbits, and that the immunological response of the experimental host to injections of killed *T. pallidum* is influenced by (1) the method of killing the organisms, (2) the number of organisms injected, (3) the species of animal used, and possibly (4) the duration of immunization.

Injections into rabbits of relatively small numbers of organisms killed by heat or by " mapharsen " (oxophenarsine) caused an appreciable rise in the treponemal immobilizing (T.P.I.) titre, standard serum tests changing from negative to positive reactions. Control injections of heated or mapharsen-treated normal testicular tissue did not elicit these responses. Of 13 rabbits tested 12 developed immobilizing antibody, and all of the 13 developed reagin after inoculation with heat-killed treponemes. It was later possible to infect the " immunized " rabbits with an intracutaneous injection of 200 living organisms, although 9 out of 12 surviving animals showed immobilizing antibody at the time of challenge.

Mice inoculated with 8×10^6 living *T. pallidum* did not develop immobilizing antibody or immunity to reinoculation within 3 months. When later 30 and 200 million heat-killed organisms were injected, although the T.P.I. titre rose, there was likewise no immunity to reinoculation.

G. L. M. McElligott

978. **Mass Treatment of Treponemal Diseases, with Particular Reference to Syphilis and Yaws**

T. Guthe, F. W. Reynolds, P. Krag, and R. R. Willcox. *British Medical Journal* [*Brit. med. J.*] **1**, 594–598, March 14, 1953. 3 figs., 24 refs.

This paper gives an account of one of the activities of the World Health Organization (W.H.O.) in the investigation of a group of diseases due to infection with closely related treponemes, the acute and chronic pathological conditions caused by which result in incapacitation and invalidism on such a scale as to be of considerable social and economic importance. In addition to syphilis, which is widely spread throughout the world, there are a number of important geographical " pockets " of treponemal infection, such as the " endemic syphilis " of Bosnia, Yugoslavia, Madras, Bechuanaland, and Tahiti, " njovera " of Southern Rhodesia, " bejel " (a non-venereal treponemal infection of children in the Eastern Mediterranean area), and yaws and pinta, which are confined to tropical and semi-tropical regions. Unfortunately in all these areas facilities for serodiagnosis are extremely inadequate and likely to remain so. Under projects organized by W.H.O. during a period of less than 3 years, 9,000,000 persons have been examined and over 3,000,000 treated with penicillin, which is the most efficient and safest therapeutic agent for all the treponematoses. Successful treatment has been found to depend on the maintenance of an effective plasma level of penicillin for an adequate period. For this purpose the most economical method of treatment is to give 1 to 2 mega units of procaine benzylpenicillin in oil with 2% aluminium monostearate (P.A.M.), repeated if possible after an interval of 3 to 5 days. The need for the proper standardization of P.A.M. is stressed and the minimum specifications established by W.H.O. are described.

There appears to be ample evidence that mass treatment of clinically diagnosed treponemal disease in the early stages alone will not suffice to stamp out the disease and that there must also be supplementary long-term measures if such projects are to succeed. There also seems to be a strong case for the " preventive " or " abortive " treatment of contacts, but on this point medical opinions differ. In general it is concluded that results will be far from satisfactory unless 90%of a population are examined and unless re-checking is carried out after an interval of 6 to 12 months. [It is doubtful whether this could ever be achieved without a far greater degree of cooperation of the population concerned than has yet been obtained.]

Neville Mascall

[The above article should be read in conjunction with a previous paper by two of the authors (Reynolds and Guthe, *Amer. J. Syph.*, 1952, **36**, 424; *Abstracts of World Medicine*, 1953, **13**, 114), which covers much the same ground.—Editor.]

979. **Chorioretinitis of Congenital Syphilis**

J. V. Klauder and G. P. Meyer. *Archives of Ophthalmology* [*Arch. Ophthal.* (*Chicago*)] **49**, 139–157, Feb., 1953. 9 figs., bibliography.

After a full review of the literature, the authors describe an investigation at the Wills Eye Hospital, Philadelphia, into the occurrence of chorioretinitis in patients with congenital syphilis. For this purpose they studied 223 cases of congenital syphilis with interstitial keratitis and also 71 cases of congenital syphilis without corneal involvement. The great majority of the 223 patients in the former group were between the ages of 8 and 25 years; in the latter group were 54 children without any ocular complaint, and 17 patients (mostly adults) having some ocular involvement. Of the subjects with

keratitis, 30 had signs of chorioretinitis and 18 had perivascular sheathing. Of patients without keratitis, 12 had choroidal scarring and 8 had perivasculitis.

According to the authors, the chorioretinal scarring did not fall easily into the 4 types described by Sidler-Huguenin. The main feature was pigmentary disturbance, either granular or in annular zones. Changes resembling retinitis pigmentosa were found in 3 cases only, none of them associated with keratitis. Macular involvement occurred bilaterally in 3 and unilaterally in 6 of the 42 patients with chorioretinitis. The authors consider that the 26 cases with perivascular sheathing provided a large enough group to justify the recognition of this manifestation as a valuable diagnostic sign.

J. E. M. Ayoub

980. **Penicillin Treatment of Cardiovascular Syphilis**
H. BEERMAN. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **29**, 18–31, March, 1953. Bibliography.

The results of treatment of cardiovascular syphilis with penicillin, as reported in the literature, are reviewed and the statistical difficulties in their evaluation are stressed. It is also pointed out that groups of cases treated by different observers are seldom strictly comparable, differences of occupation and race being particularly important in relation to cardiovascular disease. It is emphasized that the best results are to be anticipated in those patients who are treated in the pre-symptomatic phase. In a detailed consideration of the problem of therapeutic shock during the penicillin treatment of cardiovascular syphilis the views of those workers who believe that the importance of this reaction has been exaggerated receive prominence.

The author concludes that while the clinical results of penicillin treatment are promising on the whole, the serological results are disappointing, and it is suggested that co-existent neurosyphilis, which is not infrequently present, may in part be responsible for this. It is also concluded that as severe reactions to penicillin are relatively rare, the drug may be used safely in those cases of cardiovascular syphilis in which, in the past, arsenicals were contraindicated. Preliminary medication with bismuth and iodides is not considered necessary. However, a 10-year follow-up of a large number of cases is necessary before a final opinion on the usefulness of penicillin in this condition can be formed.

R. R. Willcox

981. **Residual Non-gonococcal Urethritis: P.A.M. and Sulphathiazole in the Treatment of Gonorrhoea**
C. D. ALERGANT. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **29**, 34–35, March, 1953.

A single dose of 300,000 units of procaine penicillin with aluminium monostearate (P.A.M.) was combined with one tablet [presumably 0·5 g.] of sulphathiazole 4 times a day to a total of 20 g. in the treatment of 120 cases of acute gonorrhoea at Liverpool Royal Infirmary. Among the 46 patients who attended regularly, supplementary treatment for residual non-gonococcal urethritis was required in 12 cases (28·6%), while among 56 patients treated with P.A.M. alone the incidence was 30·4% (17 cases). The addition of the sulphathiazole thus had no effect on the incidence of residual non-gonococcal urethritis following the treatment of gonorrhoea with penicillin, nor was there any difference in its severity between the two groups.

R. R. Willcox

982. **Chloromycetin Treatment of Gonorrhea. Evaluation of a Single Oral Dose Administered to Patients with Acute Gonorrheal Urethritis**
C. D. BARRETT and M. E. BURTON. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 165–176, March, 1953. 10 refs.

Although several previous reports on the treatment of gonorrhoea with chloramphenicol have indicated the effectiveness of relatively small total doses ranging from 0·75 to 6 g., Greaves *et al.* (*J. vener. Dis. Inform.*, 1950, **31**, 261) claim to have obtained satisfactory results with a single oral dose as small as 0·75 g. In view of this finding, the present authors, in an investigation at the Venereal Disease Clinic of the Health Department of Detroit, Michigan, set out to evaluate the effectiveness of a single oral dose of chloramphenicol in the treatment of gonorrhoea, comparing their results with those obtained from the administration of penicillin.

A total of 1,718 males suffering from acute gonorrhoeal urethritis was divided into 2 groups of 904 and 814 patients respectively. In the first group 460 patients were given a single oral dose of 1 g. of chloramphenicol and 44 received penicillin; in the second group 409 patients were given 2 g. of chloramphenicol in a single oral dose and 405 received penicillin. The penicillin treatment in each case consisted of a single intramuscular injection of 300,000 units of procaine penicillin in oil with aluminium monostearate. Patients were examined 1, 2, 3, 7, and 15 weeks after treatment, but the difficulty of deciding " reinfection " or " failure " at 7 days prompted the authors to carry out the first post-treatment examination after 2 days in the later cases under review.

Between 50 and 60% of patients in each group reported for follow-up examination. At the end of one week negative urethral cultures were found in 88·7% of patients receiving 1 g. of chloramphenicol and in 93·3% of those receiving 2 g., whereas in the penicillin-treated series the figures were 97·4% and 96·6% respectively. In this connexion the authors stress the importance of cultural as against purely clinical evaluation of results.

No serious side-reactions occurred in any of the groups, though some patients complained of mild gastro-enteritis, dizziness, or " bad taste ". The risk of the development of aplastic anaemia after repeated or indiscriminate administration of chloramphenicol is stressed. In instances of undoubted reinfection, cure was obtained by re-administering the same drug, suggesting that the gonococci were not resistant to the particular drug used in these cases.

The authors conclude that while penicillin remains the drug of choice in the treatment of acute gonorrhoea, the nearly similar results obtained with oral administration of 2 g. of chloramphenicol suggest that this drug may be substituted for penicillin when the latter is not available or is contraindicated.

Douglas J. Campbell

Allergy

983. **The Relationship of Experimentally Produced Asthmatic Attacks to Certain Acute Life Stresses**
D. H. FUNKENSTEIN. *Journal of Allergy* [*J. Allergy*] **24**, 11–17, Jan., 1953.

The effects of mental stress on the reaction of asthmatic patients to methacholine was studied at Harvard Medical School. The subjects, 8 male students known to be suffering from frequent asthmatic attacks but who had had none during the previous 4 weeks, were given injections of 10 mg. of methacholine intramuscularly during a period of their college life when they were under no unusual stress, and again on the evening before a final examination. The degree of stress and the asthmogenic effect of the injection were estimated clinically and subjectively, and an attack induced was classed as " severe " or " mild ". Before the examination the drug provoked a mild attack in 5 cases and had no effect in 3 cases, whereas during the control period severe attacks were provoked in all 8 cases.

[This interesting result would have been of more value if respiratory function had been measured during the attacks.] *H. Herxheimer*

984. **The So-called Angioneurotic Edema**
E. BRUUN. *Journal of Allergy* [*J. Allergy*] **24**, 97–105, March, 1953. 31 refs.

Of 132 patients with so-called angioneurotic oedema (most of whom were between 30 and 50 years of age and two-thirds of whom were women) seen at the Allergic Diseases Out-patients' Clinic, University of Copenhagen, in 73 it could be shown to have an allergic aetiology. This was verified by at least two criteria of the following four: history, exposure test, skin test, and effect of desensitization. Of these 73 allergic patients, 38 were cases of drug allergy, due mainly to aspirin (24) or barbituric acid (5). In 18 cases food allergy was found (shellfish 3, fruit 3, eggs 2), while in a further 11 cases contact or inhalant allergy was the cause. As the majority of the patients did not show any " neurotic " aetiology, the author suggests that the term angioneurotic oedema should be replaced by the term allergic oedema, or angio-oedema, as proposed by Cooke. *H. Herxheimer*

985. **Detection of Antibodies in the Serum of Patients Suffering from Hay Fever.** [In English]
E. S. ORLANS, L. J. RUBINSTEIN, and J. R. MARRACK. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **6**, 33–43, 1953. 1 fig., 12 refs.

A controlled investigation was carried out at the London Hospital to determine whether antibodies against constituents of grass pollen were present in the serum of patients suffering from hay-fever, Boyden's technique being used in which tanned erythrocytes absorb protein on their surface and are agglutinated by homologous antisera. Antibodies were found in the serum in about one-third of untreated cases of hay-fever, and in the serum of all patients who had had a full course of treatment with pollen extract. No antibodies were found in the serum in the controls. The amount of antibody in treated subjects was not related to the results of treatment, though a relatively low titre was observed in the serum of untreated controls. It is suggested that as there was no relationship between the strength of the antibody and the clinical results of treatment, the antibodies detected were not antibodies against the allergen of the pollen.
A. W. Frankland

986. **Pregnancy and Allergic Diseases.** [In English]
K. JENSEN. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **6**, 44–53, 1953. 16 refs.

Until recently it was widely held that asthmatic symptoms were not aggravated by pregnancy; indeed some workers have reported that symptoms improved during pregnancy. The present authors, working at the University of Copenhagen, have studied the influence of pregnancy on 72 patients, 49 of whom had bronchial asthma, 11 vasomotor rhinitis, and 12 bronchial asthma with vasomotor rhinitis. It was found that during pregnancy symptoms improved in 28, were unchanged in 14, and became worse in 30. Improvement generally occurred at the beginning of pregnancy and ceased immediately after delivery. Aggravation of symptoms, on the other hand, was observed at any time. In the 24 multiparae in the series the response was alike in the first and subsequent pregnancies, that is, if symptoms improved in the first they were not aggravated in a later pregnancy, and if the asthmatic symptoms became worse during the first they did not improve in a subsequent pregnancy. *A. W. Frankland*

987. **ACTH in Gelatin. Clinical Results with Repository Adrenocorticotropic Hormone in Allergic Diseases**
S. J. LEVIN. *Annals of Allergy* [*Ann. Allergy*] **11**, 157–169, March–April, 1953. 15 refs.

In an investigation of the results of treatment with repository ACTH in allergic diseases at the Children's Hospital of Michigan and the Wayne University School of Medicine, Detroit, Michigan, 37 allergic patients, 16 of whom were suffering from severe asthma, were given ACTH in gelatin intramuscularly. Usually 40 to 60 mg. was given daily for the first 2 days, then 20 to 40 mg. on the 3rd day, and 20 mg. if necessary on each of the 4th, 5th, and 6th days. Treatment was then discontinued without further tailing off. This form of treatment was used to transform the severe character of the allergic state into a milder form, and was followed by the routine methods of anti-allergic treatment.

Local or general side-effects were absent, and the therapeutic effect was classed as either " excellent " or " good " in all cases. *H. Herxheimer*

Nutrition and Metabolism

988. **Effect of Emulsifiers on Fat Absorption in the Normal Young Adult**
H. C. TIDWELL and M. E. NAGLER. *Gastroenterology* [*Gastroenterology*] **23**, 470–476, March, 1953. 17 refs.

In experiments at the University of Texas, Dallas, the authors investigated the effect of adding an emulsifying agent to the diet both of human subjects and of rats, it having been suggested that emulsifiers may influence fat absorption. They found that the ingestion of an exogenous emulsifying agent did not cause any significant alteration in the chylomicrographic curves of 12 healthy medical students; and that the addition of " tween 80 " or glyceryl mono-oleate as a 6% supplement to a standard fat meal in rats did not significantly affect fat absorption, fat splitting, or gastric or intestinal motility.

From these results they are led to conclude that the natural emulsifying mechanism is already optimal from the point of view of absorption. *A. C. Frazer*

989. **Observations on the Vitamin A Tolerance Curve as an Index of the Degree of Fat Absorption**
C. W. LEGERTON, E. C. TEXTER, and J. M. RUFFIN. *Gastroenterology* [*Gastroenterology*] **23**, 477–481, March, 1953. 2 figs., 14 refs.

The authors, at Duke University School of Medicine, Durham, North Carolina, have studied fat absorption as measured by fat balance and correlated the level of absorption with vitamin-A absorption curves in 27 subjects—8 with sprue, 4 with chronic pancreatitis, 1 with Whipple's disease, 3 after gastric resection, 3 after intestinal resection for regional ileitis, and 8 without gastro-intestinal disease. They claim that the vitamin-A absorption curves parallel the over-all level of fat absorption. [It is clear, however, that flat vitamin-A curves occur when the over-all fat absorption is 75% of normal or below.] *A. C. Frazer*

990. **Intravenous Alcohol Therapy.** (Erfahrungen mit der intravenösen Alkoholtherapie)
G. GRUNDMANN. *Helvetica chirurgica acta* [*Helv. chir. Acta*] **20**, 60–71, March, 1953. 28 refs.

The authors report their experience of the intravenous infusion of alcohol in 964 cases at the University Surgical Clinic, Tübingen. A 7 to 10% solution of ethyl alcohol was given at a rate of 40 to 80 drops per minute, 1,500 to 2,500 ml. (100 to 180 g. of alcohol) being given in 24 hours. With this rate of administration the concentration of alcohol in the blood reached a level of 0·3 to 1·0 part per thousand (30 to 100 mg. per 100 ml.). Analgesia and hypnosis in postoperative cases were satisfactory, and no morphine was required in addition. Furthermore, alcohol provides an efficient source of energy, its caloric value being 7·13 Cal. per g. The narcotic effect, with the concomitant danger of addiction which makes alcohol an unsuitable therapeutic agent in the majority of patients, was reduced by the simultaneous administration of glucose (20%), which enhances its combustion, while the caloric deficit in the postoperative period would cause a further increase in the rate of combustion. Usually about 1,900 Calories were supplied daily in the form of alcohol and glucose.

It is also claimed that alcohol given in this way enhances the antiketogenic effect of carbohydrate, and has a stimulating effect on circulation and respiration, a diuretic effect, and a sialogogic effect. Toxic effects were giddiness, nausea, vomiting, torpor, and eventual excitement. Children were excluded from this form of treatment, while patients suffering from epilepsy, gout, and atherosclerosis were also regarded as unsuitable. The danger of liver damage is not great with administration over a short period. As the infusion of a highly concentrated fluid is liable to give rise to thrombosis of the veins, the site of administration was changed every 24 hours. *A. C. Frazer*

991. **Preparation for Operation and Postoperative Parenteral Nutrition with Ethyl Alcohol.** (Präoperative Vorbereitung und postoperative parenterale Ernährung mit Äthylalkohol)
Z. SEIWERTH. *Helvetica chirurgica acta* [*Helv. chir. Acta*] **20**, 72–82, March, 1953. 2 figs., 14 refs.

During the past 2 years 250 patients at the University Surgical Clinic, Skopje, Yugoslavia, have received intravenous infusions of a 5 to 10% solution of ethyl alcohol (95%), usually with 5 to 10% of glucose, in preparation for operation and during the postoperative period. The amount of alcohol given was usually determined from the caloric requirements of the patient as calculated from du Bois's tables. If the alcohol was infused continuously in a quantity sufficient to supply the whole caloric requirement, a slight rise of the blood alcohol level to about 40 mg. per 100 ml. occurred, while if double this amount was given, a level of 70 to 80 mg. per 100 ml. was reached within the first hour, only a slight further rise occurring subsequently. This level usually sufficed for the production of analgesia and euphoria. On the average, 16 ml. of 95% alcohol in 160 to 320 ml. of saline per hour was required for this purpose. It is claimed that alcohol is superior to morphine for postoperative use, as respiratory depression occurs only when very large amounts have been given. Its dilator effect on the coronary arteries makes it a suitable analgesic in cases of angina pectoris, while postoperative complications of the gastro-intestinal tract, such as paralytic ileus, meteorism, and intestinal spasms, are said to occur less frequently after this form of treatment. Inebriation occurs only when the blood alcohol level exceeds 100 mg. per 100 ml.

In the series of cases reported here, alcohol infusions were given before operation and for the first 3 days after operation. Preoperative medication was especially valuable for the anxious type of patient. The total

amount of fluid infused in 24 hours amounted to 3 to 4 litres, containing 150 to 200 ml. of 95% alcohol, 200 to 250 g. of dextrose, 1 g. of protein [form not stated] per kg. body weight, about 10 g. of sodium chloride and 3 g. of potassium chloride, ascorbic acid, and the vitamin-B complex. The alcohol did not interfere with the utilization of the vitamins. Up to 2,100 Calories could be administered in this way daily and a positive nitrogen balance attained, while the average loss of weight as a result of the operation was less than that in a control group of patients who were given infusions of fluid containing the same ingredients apart from the alcohol. Thrombosis of the veins occurred invariably if the 10% solution was used. Patients with any form of mental disease or with epilepsy were excluded from this treatment, as were cases of severe sepsis and of liver disease. Shock was also regarded as a contraindication, owing to the vasodilator effect of the alcohol. *A. C. Frazer*

992. **Lesions of Mucocutaneous Junctions in the Rat in Deficiency of Pyridoxine**
V. RAMALINGASWAMI and H. M. SINCLAIR. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **20**, 81–92, Feb., 1953. 10 figs., 20 refs.

Ever since lesions of mucocutaneous junctions in association with pellagra were first described in 1912, they have been variously ascribed to lack of some one of a number of specific factors, including pyridoxine. The present authors state: "It is difficult to assess the specificity of lack of these nutrients in the causation of mucocutaneous lesions in man, as so many uncontrollable factors limit their significance in clinical experiments. It is therefore essential to supplement clinical observation by the test of animal experimentation in which these limiting factors can be controlled or equalized between the deficient and controlled groups".

In experiments carried out at the Laboratory of Human Nutrition, Oxford, perfect control was established, the object of the investigation being to determine the effect of pyridoxine deficiency in rats.

A vitamin-free basal diet supplemented by weighed amounts of aneurin hydrochloride, riboflavin, nicotinic acid, calcium pantothenate, biotin, inositol, choline chloride, *para*-aminobenzoic acid, pteroylglutamic acid, vitamin K ("synkavit"), vitamin A, calciferol, and alpha-tocopherol acetate was given to 24 female rats 11 weeks old. The animals were divided into two equal groups, each group including the same number of litter mates. In the control group, which received 0·1 mg. of pyridoxine daily, no signs of pyridoxine deficiency developed. In the experimental group clinical signs were observed in the 14th week, the earliest being a mild erythema and fine scaliness of the hind paws and digits. Changes in the nose appeared either simultaneously with, or within 2 or 3 weeks of, the changes in the skin of the paws. The lips and angles of the mouth were involved soon after or, in some instances, not until the 16th to 18th weeks, the angles of the mouth being affected earlier and more frequently than the lips. Later still, about the 20th week, lesions in the perianal and periurethral areas were observed, with, in 6 of the 12 "deficient" rats, a scaly, oedematous condition of the eyelids and, in 2 animals, some scabbiness of the ears. The tongue, conjunctiva, and cornea were unaffected. When pyridoxine was give to 4 "deficient" animals reversal of the changes was obvious within 72 hours and was complete in two weeks.

The histological changes in 8 "deficient" animals killed in the 24th week are described and illustrated. The photographs of the animals showing angular stomatitis, cheilosis, and perianal lesions serve to demonstrate the close resemblance between these lesions in animals and in man. The authors conclude that "pyridoxine is essential for the integrity of the mucocutaneous junctions in the rat as may well be the case in man".

H. S. Stannus

993. **Management of Intractable Sprue with Cortisone and Adrenocorticotropin (ACTH)**
H. COLCHER, S. R. DRACHMAN, and D. ADLERSBERG. *Annals of Internal Medicine* [*Ann. intern. Med.*] **38**, 554–567, March, 1953. 2 figs., 10 refs.

The authors report from the Mount Sinai Hospital, New York, the treatment of 8 cases of intractable primary sprue in 4 men and 4 women, of whom 7 had non-tropical sprue and the 8th tropical sprue. In 7 of the cases previous treatment with vitamins given parenterally and orally, "tween 80", pancreatin, bile salts, plasma, and blood transfusions had given equivocal results. Diarrhoea, loss of weight, and steatorrhoea were present in all cases, and anaemia and other haematological disorders persisted. ACTH was given only to patients in hospital, treatment after discharge being changed to cortisone. The initial dose was 100 mg. daily for both drugs.

A number of complications were seen. Overt tetany occurred in 4 cases, and was believed to be due to hypochloraemic alkalosis; it could be prevented by the administration of ammonium chloride. Oedema occurring early in treatment sometimes required mercurial diuretics for its control. In all, 13 courses of cortisone and 8 of ACTH were given. Striking clinical improvement in a few days occurred in 5 patients, and although no change in the haematological findings was noted, the diarrhoea disappeared promptly and there was a substantial increase in weight. In 4 cases the vitamin-A absorption curve improved. Some degree of clinical remission occurred in all cases, but clinical relapses invariably occurred 1 to 5 weeks after cessation of therapy. No case of resistance to this form of therapy has developed so far, and it is hoped that the improvement can be maintained by continuous administration of small doses of cortisone. *C. L. Cope*

994. **Cystine Storage Disease with Aminoaciduria and Dwarfism (Lignac–Fanconi Disease).** [In English]
H. BICKEL, H. S. BAAR, R. ASTLEY, A. A. DOUGLAS, E. FINCH, H. HARRIS, C. C. HARVEY, E. M. HICKMANS, M. G. PHILPOTT, W. C. SMALLWOOD, J. M. SMELLIE, and C. G. TEALL. *Acta Paediatrica* [*Acta paediat., Uppsala*] **42**, Suppl. 90, 1–237, 1953. 33 figs., bibliography.

Gastroenterology

995. **Transduodenal Sphincterotomy for Chronic Relapsing Pancreatitis**
J. W. MAJOR and E. J. OTTENHEIMER. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 130–132, Jan. 22, 1953. 8 refs.

In this paper from Yale University School of Medicine only cases of pancreatitis which are not fulminating are considered. The authors record 23 such cases, with tables giving details of age distribution, location of pain, signs and symptoms, duration of condition, and diagnostic signs. The serum or urinary amylase or diastase level was positive in 8 (35%) of the cases.

On the assumption that spasm or tightness of the sphincter of Oddi is an important aetiological factor in chronic relapsing pancreatitis, sphincterotomy has been carried out as a curative measure, but as 12 of the 23 cases reported have been followed up for less than one year it is considered that no conclusions as to the merit of this operation are permissible. [Nevertheless this paper has some value in drawing attention to mild recurrent pancreatitis as a frequently overlooked cause of relapsing upper abdominal pain and persistent symptoms following cholecystectomy.]

J. Marshall Pullan

996. **Recurrent Hernias. An Analysis of 369 Consecutive Cases of Recurrent Inguinal and Femoral Hernias**
E. A. RYAN. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **96**, 343–354, March, 1953. 4 figs., 9 refs.

Recurrence of hernia after repair is still all too frequent, and in this paper the causes are discussed. Of a series of 369 cases (343 patients, 26 of the herniae being bilateral) admitted to the Shouldice Surgery, Toronto, for repair (the primary operation having been performed elsewhere), 194 (52·6%) were indirect recurrences, 167 (45·2%) direct, and 8 (2·2%) were femoral; 16 of the indirect (4·4% of the total) were sliding in type. The previous operation was judged to have been of the Bassini type in 287 cases, of the Halsted type in 75, of the Ferguson type, with the cord deep to the internal oblique muscle, in 5, and femoral in 2. Approximately one-third (36·6%) of the recurrences appeared within 6 months and were therefore attributed to bad surgery. A few were accounted for by a second hernia having been overlooked at the original operation.

Direct herniae commonly appeared at the lateral edge of the rectus muscle, and indirect recurrence, which was most frequent after the Halsted operation, was thought in many cases to be due to incomplete freeing of the neck of the sac from the transversalis fascia. Heavy work did not seem to be a major factor in hernial recurrence, and the physical characteristics of the individual had little, if any, bearing. Direct hernia predominated in the proportion of 2·5 to 1 in the once-recurrent group, and the proportion became progressively higher in patients with 2 or more recurrences, thus indicating that the site of greatest anatomical weakness is in the direct-hernia region, but emphasis is also laid on the need for careful repair of the internal ring and the structures lateral to it in sliding hernia.

Immediate postoperative ambulation on the day of operation is advocated, and the authors suggest that a recurrence rate of 1% or less is possible in recurrent hernia; the over-all incidence of recurrence in this series was 0·8%. A 10-year follow-up period is desirable in assessing results. *Guy Blackburn*

OESOPHAGUS

997. **Curling of the Esophagus**
M. ESKRIDGE and J. D. PEAKE. *Southern Medical Journal* [*Sth. med. J. (Bgham, Ala.)*] **46**, 213–220, March, 1953. 5 figs., 5 refs.

The authors report 19 cases of " curling " of the oesophagus (or " corkscrew " oesophagus), these representing 0·78% of cases in which the oesophagus was examined radiologically in 2 years in private diagnostic practice in Mobile, Alabama. Of the 19 patients, 8 were males and 11 females. Their average age was 66 years, the youngest being 49 and the oldest 84, suggesting that the condition develops in later life.

As many of the patients had other gastro-intestinal disorders, such as hiatus hernia or duodenal ulcer, and as many had no symptoms referable to the oesophagus, doubt is expressed whether the condition is related to any specific clinical picture. In a number of the patients, however, the oesophageal condition alone was considered to be responsible for the occurrence of dysphagia and pain behind the lower half of the sternum, with possible radiation to back, neck, or epigastrium. The results of treatment in the symptomatic cases were disappointing.

[This is an interesting and clear account of the condition, in which the literature is reviewed and full details of the individual cases are given.] *T. D. Kellock*

998. **Dysphagia Produced by a Contractile Ring in the Lower Esophagus**
F. J. INGELFINGER and P. KRAMER. *Gastroenterology* [*Gastroenterology*] **23**, 419–430, March, 1953. 7 figs., 7 refs.

The authors describe 6 cases seen at the Evans Memorial Hospital, Boston, Massachusetts, in which spastic contractile rings appeared in the oesophagus just above the diaphragm. All the patients were males and gave a history of sudden dysphagia while eating. The attacks were usually precipitated by certain foods, especially solid foods not sufficiently masticated. None of the patients had regurgitation between the attacks,

and only one complained of heartburn. Duodenal ulcers were definitely present in 2 cases and less certainly in a third. Radiologically, the narrowing of the oesophagus was seen to vary in different patients and in the same case at different times. The constriction was not funnel-shaped, but tended to form a clearly defined angle with the oesophageal wall, was symmetrical, and appeared at a point 2·5 to 6 cm. above the cardio-oesophageal junction and quite distinct from the oesophageal hiatus of the diaphragm.

The authors argue strongly against the condition being due to fibrotic stricture, cardiospasm, or diaphragmatic hernia. In the one case in which resection of 4 cm. of the lower oesophagus was performed the surgical specimen supported their contentions; in this there was marked muscular hypertrophy and the whole was lined with oesophageal mucous membrane, but there was no evidence of inflammation or fibrosis. The possibility of overactivity of the inferior oesophageal sphincter is discussed. In addition to the one patient subjected to operation, another obtained considerable relief from dilatation of the lower oesophagus. In the other 4 cases no special measures were taken, but the patients have learned to prevent attacks by careful mastication and the avoidance of certain foods. *J. E. Richardson*

STOMACH AND DUODENUM

999. **The Clinical Features and Significance of Perigastritis Deformans.** (Über die Klinik und Bedeutung der Perigastritis deformans)
N. MARKOFF. *Gastroenterologia* [*Gastroenterologia (Basel)*] **79**, 65–94, Feb.–March, 1953. 27 figs., 30 refs.

The author, writing from the Cantonal Hospital, Chur, Switzerland, recalls (basing his account on recent personal observation) the clinical picture of a condition, first described by various authors about the year 1910, consisting of spastic dyspepsia, with or without inflammatory adhesions, and with changes in the *x*-ray appearance of the stomach. This condition was later called perigastritis. The main characteristics are gastric pain occurring at irregular intervals and without any relation in time to meals, and continuing for many years, during which time the symptoms are sometimes severe and sometimes minimal but are never entirely absent. They consist of epigastric pains with radiation into the back, belching, regurgitation, and finally vomiting of food without bile; there may be considerable loss of weight. The pain may be severe when accompanied by spasm, as is often the case. Constipation is frequently complained of.

The differential diagnosis from carcinoma of the cardia or lower part of the oesophagus must be confirmed. In perigastritis there is no rapid progression of the changes, and the pain can sometimes be relieved by change of posture. Another condition to be considered in differential diagnosis is diverticulum of the stomach. In contrast to a traction diverticulum resulting from pulling of the stomach wall, in perigastritis there is saccular bulging of the stomach. True diverticula involve all the layers of the stomach wall, but in pseudo-diverticula there is bulging of the mucous membrane through a muscular gap. The location of the diverticulum on the posterior wall of the cardia, on the greater curvature, or near the pylorus corresponds with the perigastritic changes. When peridiverticulitis is combined with a certain amount of deformity the differential diagnosis from perigastritis deformans becomes very difficult. The prognosis of perigastritis is generally poor.

Treatment may be surgical or conservative, the latter consisting of small frequent meals, the administration of spasmolytics, and the application of heat to the epigastrium and following, in general, the usual lines of treatment of gastritis. Specific forms, due to tuberculosis or syphilis, require specific treatment. Febrile cases respond well to antibiotics. Eleven typical case histories are given, and the author points out that long continuation of the condition may lead to various forms of pancreatitis. *E. Forrai*

1000. **Failure of Surgery to Relieve Symptoms in Prolapse of the Gastric Mucosa through the Pylorus**
E. M. RAPPAPORT, A. ALPER, and E. O. RAPPAPORT. *Annals of Internal Medicine* [*Ann. intern. Med.*] **38**, 224–233, Feb., 1953. 4 figs., 10 refs.

From personal experience the authors are of the firm opinion that prolapse of the gastric or antral mucosa through the pylorus is not the cause of gastric symptoms such as have been described in the literature. These symptoms are said to be usually vague and non-specific, consisting of epigastric discomfort, nausea, and a sensation of fullness. The authors maintain that transpyloric mucosal prolapse is a relatively common radiological finding (15·5% of 1,000 consecutive cases) and occurs in the absence of digestive complaints. They regard it as being due to gastric hyperperistalsis, and consider that the cause of the symptoms, if any, is also the cause of the hyperperistalsis. They present reports of 4 cases in which resection of excess mucosa, pyloroplasty, or gastrectomy failed to cure the patient of his original complaints. *K. Whittle Martin*

1001. **Cancer of the Stomach**
H. K. RANSOM. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **96**, 275–287, March, 1953. 7 figs., 8 refs.

Of 1,264 patients with cancer of the stomach (a term applied by the author to all types of malignant tumour) seen at the University of Michigan Hospital, Ann Arbor, between 1934 and 1946, 457 were subjected to operation designed to extirpate the primary tumour. This group, comprising 351 men and 106 women, of whom 348 were aged between 40 and 65, forms the main subject of this study. There were 83 deaths in all, an operative mortality of 18·1%.

In a careful statistical analysis it is shown that oesophago-cardiectomy and total gastrectomy carried the highest mortality. In only 3 cases treated by subtotal gastrectomy was there post-mortem evidence that total gastrectomy might have given a better result. In 70% of cases there was histological evidence of invasion of

regional lymph nodes, in 33·7% of invasion of perigastric adipose or connective tissue, and in 23·6% there were both types of involvement.

In 31 cases it was found at operation that only palliative measures could be taken; half of these patients died within 6 months, the longest survival time in this group being 2½ years. Of the 343 survivors, follow-up observations showed that 96 patients (28%) were alive 5 years or more after operation. There was no convincing evidence that the age of the patient at the time of operation affected the prognosis, but regional lymph-node involvement and invasion of perigastric tissues were of importance, reducing the 5-year survival rate from 50% (the figure in those without involvement) to 16% and from 35% to 16% respectively; only 8% of patients survived 5 years or more when the regional nodes and surrounding tissues were both affected. On a normal expectation of life it was calculated that of those who might have expected to live for another 10 years, 18·7% of patients did so, while 11·8% lived for 15 years or more. The percentage of 5-year survivals in the whole group of 1,264 patients was 7·8%. The series included 2 cases of sarcoma and 12 of lymphoblastoma but, as the author points out, these numbers are too small to warrant any conclusions being drawn. *Guy Blackburn*

1002. **Crohn's Disease Involving the Stomach. A Report on Two Cases**
F. R. R. Martin and R. J. Carr. *British Medical Journal* [*Brit. med. J.*] **1**, 700–702, March 28, 1953. 4 figs., 1 ref.

The authors state that, so far as they are aware, no cases of Crohn's disease involving the stomach have been published [although Kolodny (*Ann. Surg.*, 1935, **102**, 30) described 2 cases very suggestive of Crohn's disease affecting the pyloric antrum].

In the course of 18 months the authors have treated at Bradford Royal Infirmary 2 female patients, aged 23 and 24 years respectively, who were shown at operation to be suffering from Crohn's disease of the terminal ileum with involvement of the stomach and duodenum. In addition to the typical symptoms of regional ileitis they began to suffer from anorexia, repeated vomiting, and loss of weight. Barium-meal examination revealed in both cases loss of the normal mucosal pattern and almost complete absence of peristalsis in the pyloric antrum and first part of the duodenum. In one case the stomach and duodenum were examined at laparotomy; the stomach wall appeared to be only a little thickened, but a biopsy specimen of the mucosa from the pyloric antrum was found on histological examination to contain giant cells, and the pathologist reported the presence of "a chronic granulomatous process like Crohn's disease". In neither case was a short-circuit of the gastro-duodenal lesion carried out, but in the second case a hemicolectomy was performed as the disease appeared to be confined to the terminal ileum.

There was some improvement in the first case 2 years after the onset of the disease, when radiography showed that peristalsis and a normal mucosal relief pattern had returned to the pyloric antrum and duodenum. The general condition of the second patient 18 months after the onset of the disease had deteriorated on account of persistent anorexia and vomiting. The radiological appearances are described in detail and illustrated, and show that the changes in the gastric and duodenal mucosa are not necessarily of a permanent nature. One of the main difficulties in these cases was the inability of the patient to assimilate sufficient nourishment.

Norman C. Tanner

1003. **Acute Peptic Ulcers as a Complication of Surgery**
W. V. McDonnell and J. F. McCloskey. *Annals of Surgery* [*Ann. Surg.*] **137**, 67–73, Jan., 1953. 1 fig., 19 refs.

The occurrence of acute peptic ulcer as a complication of surgical operations has received little attention in the literature. Curling in 1842 described peptic ulcers associated with burns and Cushing in 1932 described their association with lesions of the central nervous system, and very occasional reports of a similar association of peptic ulcers with surgical procedures have appeared. The authors found 8 cases of acute peptic ulcer in the records of 234 post-mortem examinations performed at Jefferson Medical College Hospital, Philadelphia, between 1945 and 1950 on patients dying within 2 months of surgical operations, neurosurgical operations being excluded. Moreover, of the 5 cases of acute peptic ulcer found among 179 patients dying from intracranial lesions, or in whom such a lesion had been a substantial factor in causing death, in 3 death had occurred during the postoperative period. The similarity of the incidence of acute peptic ulcers in post-operative deaths and deaths from lesions of the central nervous system suggests a common aetiology, and the authors suggest that in both cases the ulcers are the result of exposure to stress, causing increased secretion of ACTH, which in turn increases gastric secretion.

The eight cases of postoperative peptic ulceration are reported in detail. *R. S. Handley*

See also Pathology, Abstract 900.

LIVER AND GALL-BLADDER

1004. **Puncture Biopsy of the Liver and Pigmentary Cirrhosis.** (Ponction-biopsie du foie et cirrhose pigmentaire)
P. Harvier, J. Di Mattéo, and J. Bescol-Liversac. *Presse médicale* [*Presse méd.*] **61**, 423–426, March 25, 1953. 10 figs., 16 refs.

Puncture biopsy of the liver is the surest method of confirming the diagnosis of pigmentary cirrhosis, and in this condition is almost without risk as the liver is usually enlarged and hard. The method is contraindicated only in cases showing an obvious haemorrhagic tendency. The authors report the results of puncture biopsy in 50 cases of disorders of the liver, of which 20 were cases of pigmentary cirrhosis; in no case was there any untoward incident. For fixation they used the method of Bouin–Hollande (trichloracetic acid), as this method con-

serves the glycogen and keeps the chromolipids insoluble so that they can be demonstrated by selective staining for fat.

Their results showed that the pigment which is first disseminated in the cytoplasm of the liver cells in the form of granules gradually becomes condensed in irregular clumps and in the course of time may appear in the Kupffer cells, suggesting that the pigment is not formed in these cells but becomes fixed through " colloidopexy ". Histochemical studies, by staining with Sudan black, showed that the pigment is a lipochrome with an iron content in proportion to its age. Staining by the method of Laidlaw confirmed that *in vitro* the lipochrome is able to fix heavy metals. In pigmentary sclerosis reticular sclerosis is always present, but usually moderate in degree, while collagenous sclerosis differs in no way from that in other cirrhoses, except that there are very dense masses of pigment lying either within the liver cells or free, the cells which contained them having been destroyed. The dominant feature in pigmentary cirrhosis is the tolerance of the liver cells for the lipochrome pigment, although finally overloading of the cells with pigment results in their atrophy and degeneration. In contrast to the views of other workers the authors consider that the overloading with iron is not due to an error of iron metabolism, but that the presence of lipochrome is the essential element, and that the increase in iron is secondary to its adsorption by the lipochrome, as is the increase in copper content. The accumulation of lipochrome is a sign of " wear and tear " of the cell, but the primary trouble has to be sought for in some disturbance of cellular metabolism. The authors suggest that this hypothesis would help to explain the predominance of the pigment in other organs, as in the polyvisceral form of the disease, in cardiac pigmentation, or in pigmentation of the skin, in which the high content of lipochrome in epidermal cells causes an accumulation of melanin. *E. Forrai*

1005. **The Bile Ducts in Pancreatitis.** (L'hépatocholédoque dans les pancréatites)
J. CAROLI and J. NORA. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **29**, 575–591, Feb. 15, 1953. 19 figs., 42 refs.

The authors describe the appearance of the main biliary ducts on examination by radiomanometric methods in cases of acute and chronic pancreatitis. A 25 to 30% solution of diodone is used for injection into the biliary passages and it is emphasized that the pressure used for each radiograph should always be stated.

Personal observation of 16 selected patients with chronic pancreatitis, upon whom biopsy of the pancreas was also carried out, showed that the radiographic appearances of the bile ducts were of two distinct types. In the first type inflammatory swelling of the pancreas causes a general narrowing of that part of the common bile duct which lies within or behind the head of the pancreas, while the part of the duct above the pancreas is dilated. This type may simulate biliary cirrhosis, stone in the common duct, or cancer of the pancreas, but can be distinguished from these by radiomanometry. In the case of pancreatitis the injection fluid is only temporarily arrested by the incomplete stenosis, the end of the duct is rigid and narrow, but there is atony of Oddi's sphincter. In cases of cancer of the pancreas with jaundice the fluid cannot pass the stricture. When enlarged lymph nodes cause the narrowing the fluid will pass under extra pressure, whereupon the common bile duct resumes its normal calibre and resilience. In the first type it is often necessary to perform choledochojejunostomy with an excluded loop of jejunum. In the second type the lesion is usually in the duct at the level of the papilla and affects both the biliary and pancreatic ducts. It may be in the nature of a fibrosis, leading to chronic enlargement of the pancreas and the suspicion of cancer. Localized areas of pancreatitis seldom cause obstruction of the biliary passages. Fibrotic lesions of the papillary region may require treatment by prolonged trans-papillary drainage. The condition may be very difficult to diagnose even with the aid of biopsy and radiomanometry, but the authors mention a new test for early papillary lesions depending upon the time of appearance in the bile of bromsulphonphthalein after it has been injected intravenously [see Abstract 1006].

In acute pancreatitis, changes in the radiographic appearances of the bile ducts are less constant and less distinctive. In 3 cases out of the 12 studied by the authors there was a retropancreatic narrowing of the common bile duct with dilatation above it resembling the picture seen in the first type of chronic pancreatitis, while in 3 others there was spasm of the sphincter of Oddi. But in the remaining 6 cases the appearances of the biliary passages were completely normal.

Zachary Cope

1006. **The Time of Appearance of Bromsulphonphthalein in the Bile: a New Test for the Diagnosis of Incomplete Obstructive Jaundice and Anicteric Blockage of the Hepatic Duct.** (Le temps d'apparition de la bromesulfonephtaléine dans la bile. Nouveau test pour le diagnostic des ictères incomplets par rétention et des blocages anictériques de la voie principale)
J. CAROLI and Y. TANASOGLU. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **29**, 591–606, Feb. 15, 1953. 12 figs., 28 refs.

The authors describe a simple diagnostic test for use in cases of liver disease which consists in the determination of the time of appearance of bromsulphonphthalein (" bromsulphalein ") in the bile after intravenous injection, together with the time of its retention in the blood. The dose given is 150 mg. per sq. metre of body surface, and its concentration in the plasma is measured 15 and 45 minutes after the injection. A semi-rigid tube is inserted into the duodenum under radioscopic control before the injection and duodenal contents taken for examination every 5 minutes after the dye has been given. If the flow of bile is less than 1 ml. per minute, it is stimulated by the intraduodenal injection of 1% procaine or 33% magnesium sulphate solution. Each sample of duodenal fluid is collected in a separate tube to which has been added a few drops of 10% sodium carbonate

solution. A red-violet colour developing in the fluid after shaking indicates the presence of the dye.

The test has been carried out on normal subjects and in cases of icterogenic hepatitis, incomplete obstruction of the hepatic duct, and various types of cirrhosis. Full clinical details are given. Bromsulphonphthalein appeared in the bile in normal subjects 5 to 15 minutes after its injection. In all but 2 of the 19 cases of icterogenic hepatitis, in which there was some dye retention in the blood, the dye appeared in the bile within the normal period. In all of 10 cases of incomplete biliary obstruction with dye retention in the blood the dye took longer than normal to appear in the bile (30 to 60 minutes). In 9 cases of cirrhosis there was some dye retention in the blood, but it appeared rapidly in the duodenal fluid well within the normal time-limit and sometimes even earlier.

The authors conclude that the test is useful clinically in helping to differentiate cases in which retention of the dye in the blood is associated with parenchymal liver damage from those in which it is associated with obstruction. *B. G. Maegraith*

INTESTINES

1007. **Studies on the Relationship between Motility and Absorption in the Human Small Intestine**
A. J. CUMMINS and T. P. ALMY. *Gastroenterology* [*Gastroenterology*] **23**, 179–190, Feb., 1953. 5 figs., 16 refs.

The rate of absorption of glucose and methionine from the intestine was studied at the New York Hospital–Cornell Medical Center in 3 normal human subjects and 2 patients with sprue. The rates for both substances were increased when hypermotility was induced by the administration of "urecholine" or physostigmine. "Banthine" (methantheline), however, in doses sufficient to cause hypomotility, did not cause any significant alteration in the glucose tolerance curve, nor did banthine affect the intravenous glucose tolerance curve. The possible significance of these observations is discussed.
A. C. Frazer

1008. **Small Gut Insufficiency following Intestinal Surgery. III. Further Clinical and Autopsy Studies of a Man Surviving Three-and-a-half Years with Seven Inches of Small Intestine**
A. M. LINDER, W. P. U. JACKSON, and G. C. LINDER. *South African Journal of Clinical Science* [*S. Afr. J. clin. Sci.*] **4**, 1–22, March, 1953. 8 figs., bibliography.

This paper is the medical obituary of the extensively reported patient Toni who, following resection of the small bowel for volvulus, was left with only 6 to 7 inches of jejunum and ileum. Extensive metabolic studies have been reported previously (*S. Afr. J. clin. Sci.*, 1951, **2**, 70 and 205; *Abstracts of World Surgery*, 1951, **10**, 182, and 1952, **11**, 68). Toni lived for 3½ years on a most unsuitable diet without vitamin or fat supplementation before dying of bronchopneumonia 3 days after readmission to Groote Schuur Hospital, Cape Town. The bodily adaptive processes consisted of a rapid reduction of weight, a fall of the basal metabolic rate to −53%, maintenance of the serum calcium, phosphorus, and protein levels by drawing on the body stores, diminution of protein catabolism, hypertrophy of the duodenum and the remaining jejunum, and an increasing ability of the large bowel to accommodate enormous stool masses, amounts up to one gallon (4·5 litres) being passed at a time.

A curious finding at the post-mortem examination was pancreatic atrophy, with dilated ducts and commencing fibrosis. The condition resembled that described in infants suffering from a diet deficient in animal protein, but Toni's effective protein intake was 35 g. daily and the authors suggest that lack of secretin and pancreozymin was the cause of the pancreatic atrophy. The liver was small and fatty owing to faulty absorption of the lipotropic factors choline and methionine and the defective production of lipocaic. At no time during life was there any evidence of anaemia; nor was there any hypoproteinaemia or oedema, a finding which is in striking contrast to the sprue-like "jejuno-ileal insufficiency" syndrome caused by gastro-colic fistula, extensive regional ileitis, or multiple small-bowel strictures or pouches. The findings in this case are compared with those in the few similar cases reported in the literature. *K. Whittle Martin*

1009. **Abdominal Resection of Low Sigmoid and High Rectal Tumours.** (Внутрибрюшные резекции дистального отдела сигмовидной и верхней части прямой кишки)
S. A. KHOLDIN. *Вестник Хирургии имени Грекова* [*Vestn. Khir.*] **72**, 35–45, Nov.–Dec., 1952. 6 figs.

The author reports his experience in performing 25 anterior resections of the lower sigmoid and upper rectum for carcinoma. The success of this operation depends on the preservation of the blood supply to those parts of the gut preserved for anastomosis and on the making of a sufficiently wide excision to ensure radical extirpation of the neoplasm. The operation is contraindicated in the presence of massive invasion of the outgoing lymphatics, as retrograde metastases in the distal rectum may then be expected. The author divides the superior rectal artery if it is necessary for mobilization of the rectum.

There was no postoperative death in this series. In one patient the infection and suppuration of a retrorectal haematoma occurred and required drainage through a coccygeal incision. It is concluded that the immediate results of anterior resections for carcinoma at this site are good, but only late results—not yet available—will show the real value of this operation.

[The operative technique, which is described and illustrated by drawings, reveals no original features.]
Z. W. Skomoroch

1010. **The Value of Dihydrostreptomycin in Pre-operative Preparation of the Gut**
M. I. RIDDELL, H. S. MORTON, and E. G. D. MURRAY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **225**, 535–546, May, 1953. 4 figs., 35 refs.

Cardiovascular System

1011. **Surgical Correction of Lymphedema. Application of a New Operative Technique in Lymph Stasis and Allied Conditions**
D. H. PRATT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 888–891, March 14, 1953. 5 figs.

A classification of lymphedema has been given. Previous attempts at surgical correction usually failed. Removal of the skin 0·017 in. (0·43 mm.) thick with the electric dermatome removes the epithelium and not the lymph portion of the skin. After radical excision of all the rest of the tissue of the limb, the patient's own skin is replaced on the muscle. In 25 such operations there has been no recurrent lymphedema. The success of the operation depends on nontraumatizing removal of the skin, radical excision of all fascia and lymph components, including that of the skin, adequate preparation, sufficient blood replacement, and good support postoperatively.—[Author's summary.]

1012. **The Relation between Haemodynamic Changes and Clinical Symptomatology in 66 Cases of Mitral Stenosis.** (Les relations entre les altérations hémodynamiques et la symptomatologie clinique de 66 cas de rétrécissement mitral)
E. COELHO, J. M. FONSECA, A. NUNES, and F. BARROS. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **29**, 1035–1046, March 30, 1953. 10 figs., 25 refs.

A study was carried out at the Scolaire Hospital, Lisbon, of the haemodynamics in 66 cases of mitral stenosis, in 8 of which there was also mitral regurgitation. The purpose of the investigation was to determine the relationship between the symptomatology and the haemodynamic changes in all types of mitral stenosis considered for surgical treatment. Particular consideration was given to the problems of pulmonary hypertension, increase in total pulmonary and arteriolar resistance, the reduction in cardiac output and valvular flow, and the repercussion of these changes on the work of the right ventricle. Tracings made of right auricular pressure in these cases revealed that in 17 (25·7%) there was co-existent tricuspid insufficiency.

The diagnosis of mitral regurgitation is discussed at length and in the 8 cases in which regurgitation was also present the diagnosis was confirmed by tracings of the pulmonary " capillary pressure," which showed large-amplitude V waves coinciding with ventricular systole.

On the basis of their clinical and haemodynamic findings the authors propose a classification of cases of mitral stenosis, which they divide into 5 groups from the point of view of operability. They conclude that in many cases the decision whether to operate or not can be made only after investigation of the haemodynamic changes, as outlined in this paper, has been carried out.

A. I. Suchett-Kaye

CARDIOGRAPHY

1013. **Technical Modifications of Radiocardiography**
A. A. LUISADA, A. R. GOLDFARB, G. MAGRI, and R. SAFFIAN. *Science* [*Science*] **117**, 299–300, March 20, 1953. 1 fig., 2 refs.

Radiocardiography is a method of investigation in which the passage of radioactive blood through the cardiac chambers is recorded graphically. In the original method, described by Prinzmetal *et al.* (*Science*, 1948, **108**, 340; *Abstracts of World Medicine*, 1949, **5**, 547), a Geiger–Müller tube and radioactive sodium (^{24}Na) were used, the counts being graphically recorded by an ink-writing device. According to the present authors this method has several disadvantages, including the short half-life of ^{24}Na, the poor sensitivity of the counter, and the inaccuracy of the ink-writing device. They have therefore evolved a modified technique using radioactive iodine (^{131}I) and a bismuth gamma Geiger–Müller tube connected to a count-rate meter, the outlet of which is connected to a direct-writing electrocardiograph with 4 channels. A series of recordings were made with this apparatus on 6 anaesthetized dogs and 24 normal human subjects. In both animal and human subjects injection of the isotope was followed in 2 to 6 seconds by a large monophasic wave (R) lasting 1 to 4 seconds, followed 1 to 3 seconds later by a second monophasic wave (L). These large waves, each of which may be preceded by a smaller wave, are due to the passing of the isotope through the right and left ventricles, and it is suggested that the smaller waves may be due to passage of the isotope through the respective atria. In normal subjects 2 to 4 ventricular contractions occur during the passage of the isotope through each ventricular chamber. In some cases further waves are to be seen, of the same or a greater height than R and L, and it is tentatively suggested that these may be due to " the recurrent circulation of the isotope through the right and left ventricles after returning from several possible routes ", the shortest being the coronary, and the longest the splanchnic or lower-limb circulations.

William A. R. Thomson

1014. **Ballistocardiography. II. The Normal Ballistocardiogram**
W. B. THOMPSON, M. B. RAPPAPORT, and H. B. SPRAGUE. *Circulation* [*Circulation* (*N.Y.*)] **7**, 321–328, March, 1953. 7 figs., 16 refs.

In this work, carried out at the Massachusetts General Hospital, Boston, the relationship between the ballistocardiogram and other recorded cardiac phenomena was determined in order to establish the origin of the ballistic waves in known cardiac events. Ballistocardiograms were recorded simultaneously with electrocardiograms, phonocardiograms, and peripheral pulse pressures in a group of normal men aged between 23 and 47.

The authors recorded an initial positive deflection, which they label F. This wave is synchronous with the auricular sound in the phonocardiogram and with the " a " wave in the jugular venous pulse. This deflection may be obliterated by the preceding complex when there is tachycardia. The negative deflection G and the positive deflection H coincide with the later components of the first heart sound and the onset of the carotid upstroke. They thus represent the beginning of ventricular systole and the ejection phase. The negative wave I occurs with the anacrotic notch of the carotid pulse and with the onset of the femoral pulse, and is followed by the positive wave J, which coincides approximately with the peak of the carotid and abdominal aortic pulsations. The end of systole is marked by the negative deflection K. This is simultaneous with the closure of the semilunar valves as denoted by the second heart sound on the phonocardiogram and the carotid incisura.

A terminal positive deflection, N, was seen in all ballistocardiograms and coincided with the third heart sound and the rapid phase of ventricular filling. Between this wave and wave K inconstant L and M waves were sometimes recorded. The L wave, when present, occurs at the time of opening of the atrio-ventricular valves, as denoted by the 4th component of the second heart sound. The authors stress that the timing of such simultaneously recorded events may be rendered inaccurate by differing degrees of phase distortion, for which correction must be made. *D. Weitzman*

CONGENITAL HEART DISEASE

1015. **Six Cases of Single Ventricle with Pulmonary Stenosis**

M. CAMPBELL, G. REYNOLDS, and J. R. TROUNCE. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **102**, 99–139, 1953. 21 figs., bibliography.

In this paper from Guy's Hospital, London, 6 cases of single ventricle with pulmonary stenosis are described and 78 cases from the literature are reviewed. It is pointed out that a single ventricle with two auriculo-ventricular orifices, or a large single orifice, results from failure of the ventricular septum to develop normally. This abnormality is distinct from the apparently single ventricle that accompanies tricuspid or mitral atresia, where the septum is pushed far to the right or left to enclose a small chamber from which one or other of the great vessels arises; in these cases there is a single valvular orifice, not a true single ventricle in the anatomical sense.

On clinical examination there are no signs to distinguish cases of single ventricle with pulmonary stenosis from those of the tetralogy of Fallot, to which there is a functional similarity, and the electrocardiogram, angiocardiogram, and cardiac catheterization do not generally furnish additional information. Bundle-branch block is rare, so that despite a gross abnormality of the ventricular septum, conduction tissue is still present; a strong right ventricular picture is the rule. The atrial septum is intact in about one-sixth of the cases, and transposition of the great vessels of varying degree, with some form of pulmonary obstruction, is seen in about half the cases. [Much valuable anatomical information is given in this paper, which should be read in its entirety.]

James W. Brown

1016. **Cardiac Catheterization in Interatrial Septal Defect**

R. S. COSBY, G. C. GRIFFITH, W. J. ZINN, D. C. LEVINSON, S. P. DIMITROFF, R. W. OBLATH, and G. JACOBSON. *American Journal of Medicine* [*Amer. J. Med.*] **14**, 4–13, Jan., 1953. 25 refs.

The findings obtained by cardiac catheterization in 10 patients at the Los Angeles County Hospital with atrial septal defect uncomplicated by any other congenital defect or by rheumatic heart disease are described. In 7 of the patients there was a long history of shortness of breath; in addition, cyanosis was noted in 4 cases, but in none of them was a pulmonary systolic thrill palpated, as was the case in 4 of the 6 patients without cyanosis. Incomplete right bundle-branch block was present in 4 cases and " right ventricular hypertrophy " in the rest.

The authors emphasize the importance at catheterization of securing samples of blood from the pulmonary vein, left auricle, right auricle, and inferior vena cava. They refer to the danger of confusing atrial septal defect with anomalous drainage of the pulmonary veins into the right auricle, a condition they believe to be more common than is realized. In only 4 cases was the shunt from left to right, in 2 cases it was mixed, and in 4 it was reversed. In 3 of these last 4 cases the oxygen saturation in the femoral artery was over 79%, and in one it was 86%. Moderate pulmonary hypertension was present in one patient with right-to-left shunt, but the right ventricle and pulmonary artery were apparently not entered in the other 3.

The authors refer to the work of Selzer and Lewis (*Amer. J. med. Sci.*, 1949, **218**, 516; *Abstracts of World Medicine*, 1950, **7**, 492), who held that reversal of flow with consequent cyanosis was not a terminal complication of atrial septal defect, but that free admixture of blood through large defects was the chief factor responsible.

[Much of the value of this paper is lost because of the omission of so many of the findings on catheterization. These are given for the left auricle in 9 cases, for the pulmonary vein in 3, for the right ventricle in 6, and for the pulmonary artery in 5. Many assumptions are made, including the direction of flow in 3 of the 4 cases of right-to-left shunt.] *D. W. Barritt*

1017. **Surgical Closure of Interauricular Septal Defects**

H. SWAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 792–794, March 7, 1953. 3 refs.

The technique for the surgical closure of interatrial septal defects developed by the author and his colleagues at the University of Colorado School of Medicine (Swan *et al.*, *J. thorac. Surg.*, 1950, **20**, 542; *Abstracts of World Surgery*, 1951, **9**, 177) having been carried out in experimental animals with a sufficient degree of success, its clinical application is now reported. The operation

requires a bilateral antero-lateral thoracotomy. The pericardium is incised and the right atrial appendage opened beyond a control suture. The index finger, introduced into the right atrium, palpates the septal defect and acts as a guide for a long probe which is introduced through the tip of the left atrial appendix and is passed through the tissue of the upper edge of the defect and to the outside along the base of the index finger. A suture is attached to the probe and drawn through the heart, and a polythene disk or button slightly larger than the defect threaded on it on the right side. The probe is then again passed from left to right, this time through the tissue of the lower edge of the septal opening. The suture carrying the button is then drawn back through the heart and the two ends are pulled on from the left while the finger in the right atrium guides the button into position covering the defect. The suture ends are tied over a small elliptical button which invaginates the left appendix, holding the internal button firmly in place. The polythene button is quickly covered by fibrin and in 3 weeks is enveloped by a layer indistinguishable from endocardium. In no experimental animal did thrombosis around the disk or movement out of place occur.

An account is given of 5 cases of congenital interatrial septal defect in children in which this operation was performed. There was one postoperative death. In the earlier cases the results were not entirely satisfactory, and sufficient time has not elapsed to enable results of the more recent operations to be evaluated. It would appear, however, that considerable clinical benefit may follow the procedure, and it may well prevent the progressive enlargement of the heart that occurs in many untreated cases of interatrial septal defect.

T. Holmes Sellors

1018. **Surgical Closure of Interauricular Septal Defects**
R. E. GROSS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 795–797, March 7, 1953. 4 figs.

Although a small interatrial septal defect may be tolerated fairly well, the presence of a large opening results in a severe left-to-right shunt and will lead to early heart failure and death unless the defect can be closed surgically.

The author describes a method of treatment devised at the Children's Hospital (Harvard Medical School), Boston, which entails closure of the defect by means of a stitch or prosthesis through an opening in the right atrium. Blood loss is prevented by attaching to the edges of the incision in the atrial wall a rubber cone or " well " open at both ends and tall enough to allow the blood to rise to a height corresponding to the intra-atrial pressure without overflowing.

In more than 100 experimental operations in dogs it was found that blood rose only a few centimetres in the well and that the addition of small amounts of heparin prevented clotting. Moreover, the heart tolerated the opening satisfactorily for periods of more than an hour. Closure of interatrial openings was attempted with excised atrial muscle, plastic buttons and sheets, and simple sutures.

The operation has been carried out 7 times in children who had been shown by cardiac catheterization to have a left-to-right shunt of 6·7 to 22·3 litres per minute. A wide right thoracotomy is used and the pericardium opened. The large right atrium is exposed and, after incision, the " well " (a conical sleeve of rubber with a rigid upper rim) is attached by interrupted sutures, being held firm by a special clamp as blood rises into it. The hand is introduced into the well and the index finger is used to palpate the defect and to place and guide sutures and appliances.

In 3 cases the defect was closed with the Hufnagel button (two disks screwed together, one on either side of the opening), but these worked loose because of the absence of an adequate rim of tissue to maintain them in position, the children dying within a few weeks of operation. In another 3 cases closure was carried out with nylon or polythene sheet, cut to size and sutured to the edges of the defect; there were 2 successes and one death, the latter caused by clot forming beneath the projecting edge of the closing sheet, which had been made too large. Finally, one child was treated by suture of the opening with silk stitches; this gave an excellent result, though a small shunt still persists.

T. Holmes Sellors

DISTURBANCES OF RHYTHM AND CONDUCTION

1019. **Paroxysmal Ventricular Tachycardia Treated with Intravenous Injections of Quinidine**
L. E. JANUARY, H. E. HAMILTON, and D. W. SINTON. *Archives of Internal Medicine* [*Arch. intern. Med.*] **91**, 325–332, March, 1953. 5 figs., 25 refs.

The potentially serious nature of paroxysmal ventricular tachycardia calls for prompt measures; some patients cannot tolerate quinidine given by mouth, while it may be too long in taking effect in patients who are urgently ill. Hitherto the intravenous injection of quinidine has been regarded as dangerous, although its successful use in terminating attacks of ventricular tachycardia has been reported in the literature on a number of occasions.

At the State University of Iowa Hospitals during the past 12 years intravenous quinidine lactate or gluconate (65 to 650 mg.) has been used in treating 28 attacks in 11 patients. Six of these cases are described in detail. An immediate response occurred in 24 attacks, with dramatic clinical improvement in 18 of these, a delayed response occurred in 2 cases, and failure is reported in 2 cases, with the death of one already moribund patient.

The authors recommend dilution of the 10-ml. ampoules of quinidine solution (containing 65 mg.) with an equal volume of normal saline and stress the importance of injecting not more than 65 mg. of quinidine per minute. During the injection continuous ausculation and continuous direct-writing electrocardiography are carried out, any change in quality of the heart sounds, in the heart rate, or in the QRS complex being an indication for its termination. The most frequent side-effects noted were nausea and vomiting, with sweating in a

few; one patient had a convulsive seizure during the injection but this was not repeated on subsequent occasions. Electrocardiograms illustrating the abrupt nature of the restoration of normal rhythm are reproduced. *R. S. Stevens*

1020. **Mechanism of Flutter and Fibrillation**
D. SCHERF, A. I. SCHAFFER, and S. BLUMENFELD. *Archives of Internal Medicine* [*Arch. intern. Med.*] **91**, 333–352, March, 1953. 10 figs., bibliography.

The authors discuss the two principal theories of the mechanism of flutter and fibrillation, the circus-movement theory and the ectopic-focus (tachysystole) theory, and review their findings in experiments carried out at New York Medical College following the discovery that these disorders can be induced in the heart by the topical application of aconitine (Scherf, *Proc. Soc. exp. Biol. (N.Y.)*, 1947, **64**, 233).

In experimental animals fibrillation or flutter will appear within a few seconds of the application of aconitine to any part of the auricles; if the area treated is isolated from the rest of the auricle by clamping, the arrhythmia ceases except in the isolated area, but returns in both auricles when the clamp is removed. An arrhythmia thus induced can be abolished by cooling the aconitinized focus, while by cautious cooling it may be possible to transform fibrillation progressively through flutter and extrasystoles to sinus rhythm; if the cooling thermode is removed, arrhythmia returns. Stretch and pressure applied to the aconitinized area increase the rate of existing flutter, and fibrillation ensues; the arrhythmias are immediately arrested by applying potassium chloride or quinidine to the aconitinized site. By faradization or the topical application of acetylcholine to the auricle similar "tachysystolic centres" can be induced not only at the site treated, but also at a distance—usually in the sinoauricular or auriculoventricular nodes; it is not clear why aconitine does not induce such multiple centres. The authors suggest that these observations cannot be explained by the circus-movement theory, and provide strong evidence that auricular flutter and fibrillation originate in one or more ectopic foci.

The application of aconitine to any area of the ventricle of the dog induces a ventricular tachycardia indistinguishable from flutter which, as in the auricle, can be slowed or stopped by cooling the treated site. In certain cases, however, this flutter changes suddenly to fibrillation, whereupon cooling becomes ineffective. In explanation of this, the authors suggest that the tachysystolic centre set up by aconitine bombards the ventricle with rapid stimuli, causing the formation of innumerable tachysystolic centres in all parts of the ventricular myocardium, the simultaneous activity of which is seen as fibrillation. Thus ventricular fibrillation would appear to be invariably multifocal, whereas auricular fibrillation may be either multifocal or unifocal.

The characteristic feature of fibrillation, as opposed to flutter, seems to be repetitive action occurring in all parts of the myocardium in a totally irregular manner. This is apparently initiated in some way by stimuli from one or more self-sustaining tachysystolic centres, and is non-persistent in the absence of such stimuli in the auricle, but persistent in the ventricle. Thus fibrillation differs fundamentally from flutter, which appears to result from rapid stimulus-formation in a focus without the induction of repetitive action elsewhere in the myocardium.
R. S. Stevens

ENDOCARDIUM

1021. **Streptococci of the Mouth and their Relationship to Subacute Bacterial Endocarditis**
E. D. FARMER. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **46**, 201–208, March, 1953. Bibliography.

To study the relation of the streptococci present in the mouth of normal persons to those isolated from the blood of patients with subacute bacterial endocarditis, the author examined 194 strains of streptococci isolated from the mouths of 25 apparently healthy patients at the School of Dental Surgery, University of Liverpool, and found that 37% of them were identifiable as members of the Lancefield groups. Streptococci of Group H were found in 12 of the 25 patients, and of Group K in another 12. These were further investigated from a cultural and biochemical standpoint. He then examined the blood of 4 patients with subacute bacterial endocarditis, and in 2 of the 4 cases a Lancefield Group-H streptococcus was isolated from the blood. The author considers that there is sufficient evidence here to establish a possible connexion between these two sets of facts, and having regard to the transient bacteriaemia which is known to occur after dental extraction, suggests that precautions should be taken to protect the patient with a susceptible heart lesion.

[While this paper shows evidence of much careful work, the number of cases is too small to warrant any definite conclusions being drawn.] *John M. Talbot*

1022. **The Prognosis of Subacute Bacterial Endocarditis Treated with Antibiotics. Results of Treatment in 202 Cases.** (Le pronostic de l'endocardite infectieuse subaiguë traitée par les antibiotiques. Résultats du traitement de 202 cas)
E. DONZELOT, J. M. LE BOZEC, H. KAUFMANN, and J. E. ESCALLE. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **46**, 97–107, Feb., 1953. 10 refs.

The results of treatment during 1945–51 of 202 cases of subacute bacterial endocarditis are reviewed and the prognosis in such cases is discussed. Blood cultures (made in 201 of the cases) were positive in 134 cases, *Streptococcus viridans* being isolated in 67 cases, non-haemolytic streptococcus in 43, *Str. faecalis* in 15, and various organisms in the remaining 9 cases. In 67 cases (33%) no positive blood culture could be obtained after at least 5 examinations. This proportion is considerably higher than that reported by other workers, but was due to the fact that the group was heavily weighted with serious cases referred to the authors from other centres. Of the whole group, 79% had rheumatic

and 13% congenital heart disease. In 16 cases (8%) there was no evidence of previous heart disease, but the majority of these were men who had been deported to Germany during the war and in whom there was clinical or serological evidence of infection with typhus. In 14 of these the aortic valve was affected, and in 2 the mitral valve.

At first treatment was with penicillin (1,000,000 units per day), but later one of the newer antibiotics was given, the choice of drug and dose depending on the organism and on the clinical response. Of the 202 patients, 49 (24%) died within 3 months, and a further 21 (11%) within the next 7 years, giving an over-all mortality of 35%. Of the 21 delayed deaths 17 were due to heart failure; of the 132 survivors, the results were good in 120 and fair in 4; 8 patients did not reply to an inquiry.

Unfavourable features affecting the prognosis were: age under 10 (mortality 33%) or over 60 (mortality 40%); the abacteriaemic form of the disease; the presence of resistant bacteria, especially enterococci; affection of the aortic valve; the absence of previous heart disease; and the development of congestive failure. In the classic form of the disease, however, in patients between 10 and 60 years of age with compensated rheumatic disease and a positive blood culture, 83% were cured and more than 70% remained well from 4 to 7 years after the end of treatment. *Keith Ball*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1023. **Radiocirculographic Investigation of the Coronary Circulation with Radioactive Sodium Chloride.** (Radiocirculographische Untersuchung des Coronarkreislaufes mit $Na^{24}Cl$)
P. WASER and W. HUNZINGER. *Cardiologia* [*Cardiologia (Basel)*] **22**, 65–100, 1953. 13 figs., bibliography.

The authors have evolved a method of measuring the coronary arterial blood flow by means of radioactive sodium chloride injected intravenously into the right arm. The graphic record of radioactivity measured over the chest shows a major set of peaks when the radioactive substance reaches first the right and then the left side of the heart, and a minor set of peaks associated with flow through the coronary circulation back to the right heart. By this means coronary circulation time and coronary arterial flow can be calculated. There is a full description of the technique and the mathematics involved.

Determinations made by this method on 108 resting subjects with no apparent circulatory disease at the University Medical Clinic, Basle, showed that the mean coronary circulation time was $4{\cdot}2 \pm 0{\cdot}18$ seconds, and the coronary flow 6·7% of the total cardiac output. After exertion, however, when there was an increase in the heart rate, the circulation time was prolonged to 5·2 seconds and the relative flow to 8·7%. This retardation is paradoxical, as tachycardia, increased blood pressure, and coronary vasodilatation should by the laws of hydrodynamics lead to an acceleration of coronary flow. In discussing the mechanism concerned in this increase in the coronary circulation time, it is suggested that not only is the coronary bed dilated, but that possibly also additional and longer channels become opened up.

The results in patients with heart disease were in keeping with what might be expected from the clinical findings. The method is being applied in further work on the effects of drugs on the coronary circulation.
H. David Friedberg

1024. **Changes in the Leucocyte Count in Myocardial Infarction.** (Über das Verhalten der Leukocyten im peripheren Blutbild beim Myokardinfarkt)
L. SLAPAK. *Cardiologia* [*Cardiologia (Basel)*] **22**, 101–117, 1953. 3 figs., 32 refs.

The author has studied the leucocyte count in 228 cases of recent myocardial infarction seen at the Municipal Polyclinic, Vienna. Total counts were estimated daily for 6 weeks after the onset of the attack, and in 53 of the cases daily differential counts were made as well. A leucocytosis was seen in all the cases in which there was no other disease. This started on the 1st day, reached its maximum by the 8th day, and then fell rapidly. The degree of leucocytosis seemed to be correlated with the extent of the infarct; counts of over 30,000 per c.mm. were seen in 2 serious cases. In general, the smaller the leucocytosis, the better seemed the prognosis. Leucopenia was present in cases complicated by chronic rheumatoid arthritis.

The differential counts varied greatly. The appearance of immature leucocytes in the peripheral blood usually portended a grave prognosis. In most cases neutrophil granulocytes predominated in the first 2 weeks, and this was followed by a relative and absolute lymphocytosis during the 3rd week. [No explanation is offered for this.] *H. David Friedberg*

1025. **Observations on the Relationship of Pain to the Process of Myocardial Infarction, as Shown by Electrocardiographs in " Latent " Cases**
J. S. GILSON and C. M. DAY. *Annals of Internal Medicine* [*Ann. intern. Med.*] **38**, 470–477, March, 1953. 5 figs., 10 refs.

The cause of persistent cardiac pain and the electrocardiographic findings in 5 patients at the Montana Deaconess Hospital, Great Falls, Montana, who had had pain of the anginal type for prolonged periods, are discussed. In 3 of the patients the pain was related to effort, and in all it became persistent and intractable while at rest. During the period of continuous pain the electrocardiogram showed T inversion or S–T depression in lead V3, V4, or V5 ; this was interpreted as indicating myocardial ischaemia. In all 5 cases spontaneous relief of pain was accompanied by changes characteristic of infarction (S–T elevation and Q waves, progressing typically) in the leads initially showing abnormalities.

The authors believe that the persistent cardiac pain was caused by a prolonged period of ischaemia, the pain being relieved when the affected muscle was no longer viable. They suggest that this process may also occur in cases of acute infarction, and that persistence of pain should be regarded as an indication that improved myocardial

blood flow is urgently needed to prevent further death of muscle.

[Clinical details are scanty, and the evidence for eventual infarction in the second case in the series is dubious.] *J. A. Cosh*

1026. **The Diagnosis of Infarction of the Interventricular Septum**

H. L. OSHER and L. WOLFF. *American Heart Journal* [*Amer. Heart J.*] **45**, 429–440, March, 1953. 12 refs.

In 35 fatal cases of cardiac infarction proved at necropsy at Beth Israel Hospital, Boston, the electrocardiogram (ECG) was analysed in the light of the extent and severity of the pathological lesions, as revealed by injection of the coronary arteries, gross examination of the heart, and histological examination of multiple sections. Infarcts involving the septum were graded as " massive " when they extended over one-half or more of the septum, " minimal " when only a few minute patches were present in the septum, and " moderate " when the severity of the lesion lay between the two extremes. Septal involvement was present in 32 of the 35 cases, and was massive in 10 cases, moderate in 12, and minimal in 10, the left side of the septum and the free ventricular wall being always affected. Infarctions of both anterior and posterior walls were present in 25 cases, and were simultaneous in 7 of these; there was no case of perforation of the septum.

The ECG showed conduction defects in 7 of the 10 cases with massive, 7 of the 12 with moderate, and 5 of the 10 cases with minimal septal infarction. Complete left bundle-branch block occurred in 5 cases, the infarct in these being confined to the left side of the septum and being recent and massive in 2; the usual electrocardiographic signs of infarction were obscured by the branch block in all except one of the 5. Incomplete left bundle-branch block was present in 3 cases. Complete right bundle-branch block, which was associated with QRS changes indicative of infarction, occurred in 3 cases, in all of which massive transmural infarction was present; incomplete right bundle-branch block was seen in 2 cases. Complete auriculo-ventricular block occurred in 4 cases, and was associated with infarction of the postero-basal region of the septum. " High-grade auriculo-ventricular block " was present in 4 cases of infarction of the same site, but was transient or terminal. Electrocardiographic evidence of simultaneous anterior and posterior infarction was present in 2 of the 7 cases of acute infarction of the septum and adjacent anterior and posterior walls. In 8 cases QS deflection and elevation of the S–T segments were present in leads from the right side of the septum, but in one of these infarction was limited to the anterior wall of the right ventricle and did not involve the septum.

The authors conclude that a diagnosis of infarction of the interventricular septum may be made when bundle-branch block and high-grade auriculo-ventricular block occur during the course of acute myocardial infarction, when complete right bundle-branch block is associated with Q waves in the right precordial leads, and when complete left bundle-branch block is associated with Q waves over the left ventricle. *J. F. Goodwin*

HEART FAILURE

1027. **Clinical Results, Indications, and Complications of Ligation of the Inferior Vena Cava in Congestive Heart Failure.** (Résultats cliniques, indications et complications de la ligature de la veine cave inférieure dans les cardiopathies décompensées)

W. CLOETENS, D. DE MEY, and P. WIRINGER. *Acta chirurgica Belgica* [*Acta chir. belg.*] **52**, 25–37, Jan., 1953. 24 refs.

At the Anderlecht Civil Hospital, Brussels, the authors have performed the operation of ligation of the inferior vena cava below the renal arteries with right lumbar sympathectomy in 10 cases of chronic cardiac decompensation with orthopnoea, ascites, and raised venous pressure, in which control by bed rest and digitalis was becoming ineffective. Determination of the circulation time from legs to neck after the operation showed, as would be expected, a retardation (of the order of about 3 seconds). The authors claim that the patients have improved clinically as a result of this procedure, and particularly that their decompensation has once again become controllable. However, none of the patients has been followed up for longer than 11 months.

(From the discussion following the presentation of this paper it is evident that the general opinion of the Société Belge de Chirurgie was that the operation was an unnecessarily severe procedure for obtaining slight and questionable symptomatic improvement in the patient.) [This view is also taken by the abstracter.]

F. B. Cockett

1028. **The Arterial Blood Gases in Pulmonary Heart Failure**

M. M. PLATTS. *Clinical Science* [*Clin. Sci.*] **12**, 63–74, Feb., 1953. 3 figs., 11 refs.

Estimations of the oxygen saturation and carbon dioxide content of arterial blood were carried out at the University of Sheffield on patients suffering from chronic bronchitis and emphysema, with and without heart failure, and also on patients with heart failure due to other causes and on healthy subjects. It was noted that in patients with non-pulmonary heart failure these values were only slightly, if at all, abnormal. On the other hand, in patients with pulmonary disease who also had oedema and venous congestion the oxygen saturation of arterial blood was less than 72% and its carbon dioxide content more than 60 volumes %, whereas if there was no evidence of heart failure these values were over 72% and below 60 volumes % respectively but, on average, were still well outside the normal range. Successful treatment of congestive heart failure in the presence of pulmonary disease brought the arterial oxygen saturation up to about 88%, and it was thought that this level may represent the degree of permanent impairment of pulmonary ventilation which renders a patient liable to develop congestive heart failure as a result of recurrent acute infections. The administration of mercurial diuretics, which alter the acid–base balance by causing a greater urinary loss of chloride than of sodium, caused a

rise in the arterial carbon dioxide content, which therefore did not fall below 60 volumes % in some of these patients who had recovered from pulmonary heart failure but were still receiving mercurial diuretics.

Kenneth Marsh

1029. **Mercurial Diuretics: The Replacement of Parenteral Administration by a New Oral Preparation in Ambulatory Patients with Chronic Congestive Heart Failure**

S. P. DIMITROFF, M. C. THORNER, and G. C. GRIFFITH. *Circulation* [*Circulation (N.Y.)*] **7**, 380–384, March, 1953. 18 refs.

The authors report on the use of a new orally administered mercurial diuretic in 35 patients with chronic congestive heart failure. This compound is 3-(α-carboxyethyl-α-thio)-mercuri-2-methoxypropylurea, and is dispensed in enteric-coated tablets each equivalent to 10 mg. of mercury. The usual dose employed was 1 tablet 3 times per day for 2 or 3 days each week. Most of the patients were also under treatment with digitalis and low-sodium diets, and had previously received mercurial diuretics by injection.

Of the 35 patients treated (at Los Angeles County Hospital, California), 28 showed a satisfactory response, as judged by maintenance of weight and prevention of progressive failure. In 6 cases toxic effects were observed; these consisted of colic, nausea, vomiting, and diarrhoea, and occasionally a burning taste in the mouth. These toxic effects, however, were generally less marked than with other oral mercurials, because of the smaller dose required. The authors conclude that in acute or progressive failure mercury by injection is preferable, because of its more rapid action. The administration of mercurial diuretics by mouth is also contraindicated in patients with gastro-intestinal disease. *D. Weitzman*

1030. **The Distribution of the Body Water in Normal Subjects and in Patients with Cardiac Insufficiency.** (La répartition de l'eau chez l'homme normal et chez les sujets atteints d'insuffisance cardiaque)

P. A. MAURICE. *Helvetica medica acta* [*Helv. med. Acta*] **20**, Suppl. 30, 1–59, 1953. 6 figs., bibliography.

1031. **Foliandrin in Geriatric Practice.** [In English]

H. DROLLER. *Cardiologia* [*Cardiologia (Basel)*] **22**, 118–124, 1953. 5 refs.

Foliandrin is a glycoside obtained from the Mediterranean shrub *Nerium oleander*, which has a digitalis-like action, and is rapidly absorbed and rapidly excreted. In this paper from St. James's Hospital, Leeds, the author describes its use in 5 elderly patients with heart failure due to ischaemic heart disease, and in 5 chronic and 2 acute cases of cor pulmonale with failure. The dose by mouth was 0·4 mg. initially, followed by 0·2 mg. 8-hourly until the pulse rate was reduced to between 60 and 80 beats per minute; thereafter the dose was determined by results in each individual. Satisfactory results in the first group were readily obtained with oral administration, but passed off rapidly after cessation of treatment. It is considered that the drug was as efficacious as digoxin. There was a notable absence of toxic symptoms, only one patient vomiting after an experimental overdose. In the patients with cor pulmonale the results were much less satisfactory, especially in the 2 patients with the acute condition, of whom one died suddenly; in the author's view foliandrin is definitely contraindicated in acute cor pulmonale. There was no evidence to support the view that foliandrin has a bronchodilator action. *H. David Friedberg*

BLOOD VESSELS

1032. **Insidious Thrombosis of the Aortic Bifurcation. Report of Thirty-five Cases**

P. BEACONSFIELD and J. KUNLIN. *Archives of Surgery* [*Arch. Surg. (Chicago)*] **66**, 356–364, March, 1953. 4 figs., 8 refs.

In this paper from the Surgical Service of Professor Leriche, Paris, the aetiology, signs and symptoms, and treatment of thrombosis of the terminal aorta are discussed and 35 cases described.

It is pointed out that the causes of aortic thrombosis are arteriosclerosis, inflammatory arteritis, thromboangiitis obliterans, syphilis, and trauma; in some cases perivascular inflammation affects adjacent veins, lymph nodes, and nerves. The early symptoms are usually fatigue of the legs, an ache in the foot, calf, or thigh, or in the entire lower limb, low back pain, and inability to maintain an erection; there is also loss of arterial pulsation in both legs. Trophic changes in the skin or nails are seldom seen, and when present are only slight. In the late stages of the disease all the manifestations of obliterative arterial disease are observed. The onset in aortic thrombosis is insidious, in contrast to the sudden onset of symptoms due to a saddle embolus.

Without treatment the patient usually loses both legs; as thrombosis spreads upward the renal arteries become blocked, leading to uraemia. Treatment consists in bilateral lumbar sympathectomy, resection of the thrombosed segment of the aorta and iliac vessels, and amputation of dead tissue of the lower limb. Arterial resection should be undertaken unless there is severe calcification of the aorta or the periarterial inflammation binds the main vessels to adjacent tissues. The purpose of the operation is to prevent the thrombosis extending and to relieve the back pain. *J. E. Richardson*

1033. **Thrombosis of the Aortic Bifurcation Treated by Resection and Homograft Replacement. Report of Five Cases**

J. OUDOT and P. BEACONSFIELD. *Archives of Surgery* [*Arch. Surg. (Chicago)*] **66**, 365–374, March, 1953. 4 figs., 10 refs.

A new method of treating insidious thrombosis of the aortic bifurcation by resection and replacement of the bifurcation with a homograft, as developed at the Salpêtrière, Paris, is described in this paper. It is pointed out that this operation should be performed only if the patient is fit, the vessels below the block are patent, and

a homograft can be prepared, the graft being taken from a suitable cadaver not later than 4 hours after death. Details are given of 5 cases in which the operation was carried out [for the technique of which the original article should be consulted].

The early results were good and considered to be better than those of sympathectomy with resection. The authors believe that in any phase of the disease, but particularly in the advanced one which will not respond to sympathectomy, grafting should be carried out, and as thrombosis may recur in the graft or elsewhere, sympathectomy should also be performed.

J. E. Richardson

1034. **The Treatment of Intermittent Claudication with Vitamin E**

M. HAMILTON, G. M. WILSON, P. ARMITAGE, and J. T. BOYD. *Lancet* [*Lancet*] **1**, 367–370, Feb. 21, 1953. 10 refs.

The claim that vitamin E (α-tocopherol) is of benefit in the treatment of peripheral arterial disease has been investigated in controlled clinical trials at St. Mary's Hospital, London, and the Royal Infirmary, Sheffield, on 41 patients, all of whom had typical intermittent claudication of the calf muscles due to occlusive arterial disease. The patients were divided into treatment and control groups by the method of random selection. After an observation period of at least one month the patients in the treatment group were given capsules containing natural vitamin E in a dose of 450 units daily for 12 weeks; the control group received indistinguishable but inert capsules. Neither the subjects nor the investigators knew which patients were receiving vitamin E. The treatment and control groups were comparable in respect of age and of the duration and severity of the disease. The results of treatment were assessed from the patients' own impressions, by clinical examination of the limbs, and by the response to a standard exercise tolerance test in which the number of circuits over a pair of 18-inch (46-cm.) steps which the patient was able to perform before the onset of pain, and the subsequent duration of this pain, were measured. The observations were repeated at various times during the treatment and in the following 3 months.

The patients' own assessment revealed no significant difference between the groups, although 8 of the 20 patients who received vitamin E claimed to be improved, and clinical examination showed no change in either group. There was no significant difference between the treatment and control groups in the average number of circuits walked before the onset of pain. There was a slight reduction in the duration of pain after cessation of exercise in the treatment group, and a slight prolongation in the control group, but this difference was not significant.

The authors claim that other investigators, who have reported benefit from vitamin E in comparable cases, have used less strictly controlled experimental methods, and that their own results indicate clearly that vitamin E is of no appreciable benefit to patients with intermittent claudication.

[This study illustrates admirably the proper use of statistical methods, tempered with common sense, in the evaluation of clinical data. It should serve as a model for the future evaluation of therapeutic measures in intermittent claudication.] *Bernard Isaacs*

HYPERTENSION

1035. **The Natural History and Course of Hypertension with Papilledema (Malignant Hypertension)**

M. F. SCHOTTSTAEDT and M. SOKOLOW. *American Heart Journal* [*Amer. Heart J.*] **45**, 331–362, March, 1953. 47 refs.

The natural history of hypertension associated with papilloedema was studied in the records of 104 cases seen at the University of California Hospital between 1936 and 1940. The average age of the 63 men and 41 women was 42 years. There was a family history of hypertension in about one-half of the patients, and a history of significant illness (scarlet fever, frequent sore throat, glomerulonephritis, pyelonephritis, and toxaemia of pregnancy) in rather more than one-half. In 74 patients hypertension had been diagnosed 5 months to 27 years before the onset of the malignant phase. The authors estimated the average duration of the malignant phase to be 8·7 months.

Renal symptoms were observed in 87 patients, and chronic pyelonephritis was found in 12 of 37 cases in which necropsy was performed. The part played by the kidney in malignant hypertension was reflected in the response to treatment; only in those cases where renal function was good was sympathectomy or a low-sodium diet successful; in other cases the treatment of choice was administration of such drugs as hexamethonium and " dibenamine ". The rapid deterioration in renal function noted in some cases was striking, indicating the need for frequent observation of patients with malignant hypertension so that treatment may be started promptly.

In the authors' cases the appearance of papilloedema indicated a phase of the disease which, if left untreated, was usually rapidly progressive, though in 3 cases recession occurred spontaneously. A raised cerebrospinal-fluid pressure was not considered to be responsible for the papilloedema, which was sometimes unilateral. Patients with papilloedema who had impaired renal function rarely recovered. The heart was affected in nearly every case in the series. *J. L. Lovibond*

1036. **Electrocardiographic Changes in Hypertension Treated by Methonium Compounds**

A. E. DOYLE. *American Heart Journal* [*Amer. Heart J.*] **45**, 363–381, March, 1953. 9 figs., 27 refs.

Working at the University of Otago, the authors recorded serial electrocardiograms on 75 patients during treatment for hypertension with methonium compounds over periods varying from 3 to 30 months. Before treatment the tracings in 13 cases were normal, while in 62 there was evidence of left ventricular hypertrophy, which was slight in 20 and advanced in 42. As a result of treatment the signs of left ventricular hypertrophy

diminished in 57 cases, were unchanged in 16, and increased in 2. Abnormalities of the S–T segment and T wave, which were present in 54 cases before treatment, disappeared in 26 and improved in 20 cases during treatment. The QRS voltage in leads reflecting left ventricular potentials, which was abnormally high in 50 cases before treatment, returned to normal in 32 and improved in 6 cases during the treatment. The degree of improvement in the electrocardiogram was proportional to the duration of therapy—of 18 tracings taken after 3 months' treatment, only 7 showed improvement, whereas all of 40 tracings taken after 12 to 30 months' treatment were improved—and also to the reduction of blood pressure achieved and to the degree of clinical progress.

The electrocardiographic changes resulting from hexamethonium treatment are compared with those occurring after sympathectomy, to the advantage of the former. The factors concerned in the production of the electrocardiographic abnormalities in hypertension are briefly mentioned, and the author concludes that the electrocardiogram is a useful guide to prognosis and progress during treatment with hexamethonium and allied compounds. *J. F. Goodwin*

1037. **Effects of Subtotal Adrenalectomy Alone and Combined with Sympathectomy upon the Blood Pressure Levels and Complications of Severe Arterial Hypertension**
C. C. Wolferth, W. A. Jeffers, H. A. Zintel, J. H. Hafkenschiel, and A. G. Hills. *Bulletin of the New York Academy of Medicine* [*Bull. N.Y. Acad. Med.*] **29**, 115–137, Feb., 1953. 25 refs.

At the Hospital of the University of Pennsylvania the authors have performed subtotal adrenalectomy in 54 cases and total adrenalectomy in 2 others for the treatment of severe hypertension. In all but 12 cases adrenalectomy was combined with some form of sympathectomy. The amount of adrenal tissue removed was about 95%, it being found necessary for the reduction of blood pressure to produce at least a slight degree of cortical deficiency. Of the 56 patients, all of whom had failed to respond to adequate conservative measures, 13 died—2 in the first week after operation—and the remainder survived for periods ranging from 3 weeks to 14 months after operation.

The results in those patients who underwent subtotal adrenalectomy without sympathectomy were disappointing, 4 dying within 2 months and a satisfactory reduction in blood pressure occurring in only 3 cases. Of the 42 patients subjected to the combined operation, 23 have been followed up for less than 12 months; of the remaining 19, 4 have died (2 of renal failure, 2 " suddenly "), while in 4 the reduction in blood pressure was insignificant; a " satisfactory " fall in pressure was obtained in 8 cases, and a " moderate " fall in 3. The early results in the more recently treated patients appear to be at least as good. The operation has been particularly effective in patients with congestive cardiac failure complicating the hypertension, whereas in patients with impaired renal function the results have been poor.

The authors conclude that the results obtained have been sufficiently encouraging to warrant further investigation of this method of treatment, though they do not advise its adoption for general clinical use, and consider that there is at present no justification for subjecting hypertensive patients with a reasonably good prognosis to such a formidable procedure. *C. G. Rob*

1038. **Ligation of the Splenic and Hepatic Arteries in Portal Hypertension**
A. J. S. McFadzean and J. Cook. *Lancet* [*Lancet*] **1**, 615–622, March 28, 1953. 45 refs.

The term " cryptogenic cirrhosis " is given to a form of cirrhosis of the liver of obscure aetiology common in Hong Kong in which the liver is small and the seat of diffuse hepatic fibrosis, and which is invariably associated with hypersplenism. The authors discuss the surgical treatment of this condition.

Ligation of the splenic artery was performed in 5 patients, all adult Chinese males who had had at least one haematemesis from radiologically demonstrated oesophageal varices, and in all of whom diffuse hepatic fibrosis had been demonstrated by liver biopsy. None had a palpable liver, but in each case there was considerable splenic engorgement. The artery was approached through the lesser sac by way of the gastrocolic omentum, isolated at the upper border of the pancreas, tied, and cut. Further haematemeses occurred between 9 weeks and 12 months after operation in 4 of the patients, with a fatal outcome in 2. The remaining patient could not be traced.

In 7 further cases of proven diffuse hepatic fibrosis ligation of the hepatic artery, together with splenectomy or ligation of the splenic artery, was performed. All these patients had had two or more haematemeses from radiologically demonstrated oesophageal varices, and all had tense ascites, making repeated paracentesis necessary in 5 of them. Paracentesis abdominis was carried out 48 hours before operation, and a prophylactic course of penicillin, 5 mega units daily, and streptomycin, 3 g. daily, was given from 12 hours before to 7 days after operation.

In 4 cases the hepatic and splenic arteries were tied close to their origin from the coeliac axis. There was one death, which occurred on the 26th postoperative day from liver necrosis due to thrombosis of the portal vein. The oesophageal varices showed no change in one case, slight reduction in one, and disappeared in the last case. Ascites was markedly reduced in all cases, but improvement in the leucocyte and platelet counts was only temporary.

In one case splenectomy was combined with ligation of the hepatic artery close to its origin, and in 2 with ligation distal to the origin of the gastro-duodenal artery. In all 3 cases the oesophageal varices disappeared and the pancytopenia was greatly improved, as also was the ascites.

A further 8 cases of ligation of the hepatic artery, with 2 deaths due to liver necrosis, are briefly reported. In one of these the portal vein was thrombosed, but in the other it was patent. *H. F. Reichenfeld*

See also Pharmacology, Abstract 933.

Haematology

1039. **The Adrenalin (Epinephrin) Test as Applied to Hematologic Disorders**
J. B. CHATTERJEA, W. DAMESHEK, and M. STEFANINI. *Blood* [*Blood*] **8**, 211–235, March, 1953. 10 figs., 44 refs.

The adrenaline test was performed at the New England Center Hospital and Tufts College Medical School on 12 normal subjects and 63 patients with various haematological disorders in an attempt to evaluate its role in the diagnosis of hypersplenic syndromes and aplastic anaemia. Attention was directed solely to the early phase of the reaction, as it has been claimed that this phase reflects the functional activity of the spleen and bone marrow. It is concluded that a significant response with reference to any particular blood cell indicates optimum production of such cells by the formative tissue concerned and their availability in the system for mobilization in the peripheral circulation, while a poor response denotes reduced availability of the cell in question, owing either to deficient production or to peripheral destruction. The nature of a deficiency in production, whether due to aplasia, leukaemic infiltration, or maturation arrest, cannot, however, be determined by the test. The test is therefore not diagnostic of any specific disorder, and results obtained with it should always be interpreted in the light of bone-marrow and other studies. *L. J. Davis*

1040. **Plasma Thromboplastin Component (PTC). A Hitherto Unrecognized Blood Coagulation Factor. Case Report of PTC Deficiency**
S. G. WHITE, P. M. AGGELER, and M. B. GLENDENING. *Blood* [*Blood*] **8**, 101–124, Feb., 1953. 8 figs., bibliography.

The authors, working at the University of California, San Francisco, describe a case of haemorrhagic disease in a youth of 16 years in which the clinical picture simulated that of haemophilia, the whole blood coagulation time was prolonged, and prothrombin utilization was deficient. As in haemophilia, prothrombin, prothrombin conversion accelerator, calcium, and fibrinogen concentrations and platelet count were all normal and no circulating anticoagulants were demonstrable. The coagulation defect, however, was not corrected by substances known to correct the haemophilic defect (33% saturated ammonium sulphate fraction of human plasma, barium sulphate adsorbed normal plasma, and Cohn's Fraction I) but was corrected by substances which do not affect the haemophilic defect (normal serum, haemophilic plasma, 45 to 50% saturated ammonium sulphate fraction of normal plasma, citrate eluate from barium sulphate mixed with normal plasma or serum). The correction of the coagulation defect by tissue thromboplastin and platelet-poor haemophilia plasma, combined with the deficient prothrombin utilization and the normal responses to tests for prothrombin and prothrombin conversion accelerators, led the authors to conclude that the missing factor was concerned with the production of thromboplastin in the plasma. For this factor they suggest the term "plasma thromboplastin component" (P.T.C.). Such P.T.C.-deficient plasma corrects the coagulation defect of haemophilia. A method for the isolation and concentration of the P.T.C. factor is described. *A. C. Kennedy*

1041. **Hemorrhagic Diathesis due to PTC (Plasma Thromboplastin Component) Deficiency**
J. H. LEWIS and J. H. FERGUSON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **82**, 445–448, March, 1953. 1 fig., 10 refs.

The cases are described of 3 males, all of whom had a haemorrhagic tendency resembling haemophilia clinically and in prolongation of coagulation time and abnormal prothrombin consumption. Factors V and VII were present in their blood in normal amounts. Addition of normal or haemophilic plasma to the blood of these patients reduced the clotting time, while the addition of fractions of normal plasma containing the plasma thromboplastin component (P.T.C.) (see Abstract 1040; also Aggeler, *Proc. Soc. exp. Biol.* (*N.Y.*), 1952, **79**, 692; *Abstracts of World Medicine*, 1952, **12**, 425) corrected the coagulation defect in these patients but not in haemophiliacs. [No mention is made in this paper of the relationship of this P.T.C. to the "Christmas" factor of Biggs *et al.* (*Brit. med. J.*, 1952, **2**, 1378), which is also a plasma thromboplastin component, absence of which produces a haemophilia-like disease.] *A. Brown*

1042. **Haemophilia with Respiratory Obstruction**
A. C. MACDONALD, J. G. ROBSON, and H. WAPSHAW. *British Medical Journal* [*Brit. med. J.*] **1**, 1144–1146, May 23, 1953. 10 refs.

1043. **Iron Deficiency in Polycythaemia.** (Eisenmangel bei Polycythämie)
H. GOLDECK and D. REMY. *Klinische Wochenschrift* [*Klin. Wschr.*] **31**, 155–157, Feb. 15, 1953. 8 refs.

The occurrence of hypochromia without obvious cause, but which was improved by the oral administration of iron, is described in 4 cases of polycythaemia vera treated at the University Medical Clinic, Hamburg. The possible existence of relative iron deficiency was supported in these cases by the finding of low serum iron levels, and in 3 further cases by evidence of increased iron absorption after giving a test dose of iron by mouth. In 2 patients evidence of iron deficiency disappeared spontaneously when the polycythaemia was controlled by treatment with radioactive phosphorus. The possibility of endogenous iron deficiency in such cases, in which it

might be conditioned by erythropoietic hyperplasia, is discussed. The risks involved in treating polycythaemia by over-enthusiastic venesection are emphasized, and the beneficial effect of the administration of iron in certain cases is pointed out. *Mary D. Smith*

1044. **Chronic Lymphatic Leukaemia Associated with Malignant Disease**
O. D. BERESFORD. *British Journal of Cancer* [*Brit. J. Cancer*] **6**, 339–344, Dec., 1952. 10 refs.

An associated malignant lesion was found in no fewer than 20 out of 106 cases of chronic lymphatic leukaemia seen at cancer clinics in Saskatchewan, Canada, since 1932. Where the diagnosis of lymphatic leukaemia was doubtful, bone-marrow examination and lymph-node biopsy were carried out. The existence of malignant disease was confirmed histologically in 19 cases, the distribution of the carcinomata being as follows: skin and lip, 10 cases; stomach, 3 cases; breast, 2 cases; and prostate, rectum, bladder, and lung, one case each. Melanotic sarcoma was found in one case.

The author points out that the incidence of malignant disease in this group of cases of lymphatic leukaemia is the highest so far reported; this he attributes to the high incidence of cancer of the lip and skin in Saskatchewan and to the high average age of the patients in this series. It is suggested that routine blood counts on old people, particularly those referred for malignant disease, would reveal many unsuspected cases of chronic lymphatic leukaemia. *T. M. Pollock*

ANAEMIA

1045. **Specificity of Auto-antibodies in Hemolytic Anemia**
I. DAVIDSOHN and A. OYAMADA. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **23**, 101–115, Feb., 1953. 19 refs.

At the Mount Sinai Medical Research Foundation and Hospital, Chicago, the authors studied 88 patients with various forms of haemolytic anaemia, with particular reference to the antiglobulin (Coombs) test and to the presence of warm and cold auto-agglutinins. The antiglobulin test gave a positive reaction in 32 out of 33 patients with idiopathic acquired haemolytic anaemia, in 14 out of 28 patients with symptomatic haemolytic anaemia, and in 3 out of 14 patients with hereditary spherocytosis. Warm auto-agglutinins were demonstrated in the serum in 20 (61%) of the idiopathic acquired cases and in 7 (25%) of the symptomatic cases.

In the tests for warm agglutinins in the serum the authors used erythrocytes from several sources, including the patient's own cells, cells of the same blood group and Rh type, and Group-O erythrocytes of the same Rh type. Titrations were carried out with each variety of cell in 20% albumin as diluent, and also in saline after treating the cells with papain. Three reaction patterns were observed: (1) in 11 cases there were no significant differences in the reaction between the various types of cell; (2) the serum of 4 patients agglutinated the patient's own erythrocytes to far higher titres than normal cells; (3) the serum of a further 11 patients agglutinated the patient's cells but failed to agglutinate normal cells. The authors consider that previous sensitization *in vivo* was insufficient to explain the increased sensitivity *in vitro* of the patients' own erythrocytes to antibodies in their own serum.

[The concept of a strictly specific auto-antibody is an interesting one. However, if the antibodies of acquired haemolytic anaemia are sometimes strictly autospecific, as the authors claim, normal blood should survive well *in vivo* after transfusion in such cases. That this is not so is shown by the fact that one of their own patients is reported to have received 100 blood transfusions in 5 months.] *J. V. Dacie*

1046. **Development of Pigmentary Cirrhosis in Cooley's Anemia**
J. HOWELL and J. P. WYATT. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **55**, 423–431, May, 1953. 2 figs., 11 refs.

1047. **Crystalline B_{12} Inhalation Therapy in Pernicious Anemia**
R. W. MONTO, J. W. REBUCK, and M. J. BRENNAN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **225**, 113–119, Feb., 1953. 7 figs., 6 refs.

Since the effectiveness of parenteral administration of vitamin B_{12} (cyanocobalamin) in pernicious anaemia, as compared with oral or sublingual administration, is attributable to the ready access of the vitamin to the capillaries, it was considered possible that inhalation therapy might prove equally effective. The dosage used was the same as that given parenterally, a solution of crystalline vitamin B_{12} in saline (15 μg. per ml.) being given in 2 cases by means of a nebulizer, while a third patient inhaled a dust of lactose powder mixed with the vitamin. None of the patients developed signs of toxicity or sensitivity to the vitamin. The detailed case reports show that satisfactory haematological responses were obtained and that the dosage levels required were considerably below those necessary for oral administration. *H. Payling Wright*

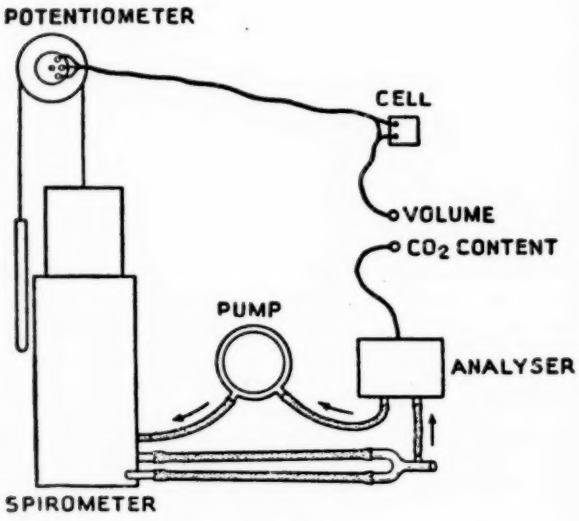
1048. **The Physiopathology of the Erythroblast in the Anaemia of Chronic Renal Failure.** (Physiopathologie des érythroblastes dans l'anémie des azotémies chroniques)
C. SACCHETTI. *Acta haematologica* [*Acta haemat.* (*Basel*)] **9**, 97–106, Feb., 1953. 4 figs., bibliography.

In 6 cases of chronic glomerulonephritis with evidence of renal failure and normocytic, hypochromic anaemia the activity of erythropoiesis in tissue cultures of the bone marrow was studied by the determination of mitotic indices and maturation curves. Marrow grown in a medium containing plasma from the same patient showed much less proliferation than when plasma from a healthy person was used, maturation of the erythroid series also being slower and less vigorous. This myeloid asthenia in chronic nephritis is well known and is usually not affected by any form of treatment. [A good account of this a-regenerative anaemia in nephritis is given by Leitner (*Bone-marrow Biopsy*, London, 1949)].
E. Neumark

Respiratory System

1049. **Automatic Fractional Analysis of Expired Air as a Clinical Test**
A. C. DORNHORST, S. J. G. SEMPLE, and I. M. YOUNG. *Lancet* [*Lancet*] **1**, 370–372, Feb. 21, 1953. 4 figs., 5 refs.

In this paper from St. Thomas's Hospital, London, is described the use of a commercial analyser for continuous recording of the carbon dioxide content of expired air. The apparatus is shown diagrammatically below.



The carbon dioxide content of expired air was estimated 3 times per second; throughout the respiratory cycle and a virtually continuous record obtained. Intrathoracic pressure and trunk expansion were recorded simultaneously in some cases.

In healthy subjects the CO_2 content of expired air increased by about 0·5% during forced expiration of 1 to 2 litres, the graph recorded being straight and gently sloping and the rate of increase being independent of the rate of expiration. In emphysematous subjects during similar forced expiration the CO_2 content increased by 2 to 4%; the rate of increase in these cases, however, diminished during expiration *pari passu* with the diminishing rate of expiration. This part of the investigation was considered to confirm previous work on the poor spatial correlation between ventilation and perfusion in emphysematous lungs.

In hypertensive cardiac failure and in asthma the patterns were normal; in gross chest disease (such as bronchiectasis) without emphysema they were intermediate. A bronchodilator spray produced no improvement in the CO_2 curve in any of the patients; indeed, the increase was sometimes greater because the patient emptied his chest better. In the case of an emphysematous asthmatic patient no change in the emphysematous curve was noted during an attack of asthma. The authors consider that this procedure constitutes a practical clinical test for emphysema. *Bernard Freedman*

1050. **" Adenoma " of the Trachea and Bronchi**
N. R. BARRETT and R. H. THOMLINSON. *St. Thomas's Reports* [*St Thom. Rep.*] **8**, 5–19, 1952. 27 figs.

The authors, in reporting 34 cases of " adenoma " of the air passages seen during a period of 20 years at St. Thomas's Hospital, London, point out that the term " adenoma " is unsatisfactory, as these tumours form a distinct group: although clinically they run a benign course, histologically they appear to be malignant. It is considered, however, that provided the nature of these tumours of the trachea and bronchi is understood, the term " adenoma " may be retained, as long as it is placed between inverted commas to indicate that it is not a true description. Of the 34 cases, the tumour was situated in the trachea in 3, in the main or a segmental bronchus in 22, and peripherally in 8. Treatment was as follows : pneumonectomy in 9 cases, lobectomy in 17, thoracotomy and local excision in 2, and endoscopic removal in 4. In only one case was there a recurrence of the tumour, arising in mediastinal nodes following lobectomy. One elderly patient was treated conservatively. [In both sets of figures given above one case is unaccounted for.]

The pathology of bronchial " adenomata " is discussed in detail. The authors consider it probable that these tumours change slowly over a course of years until eventually infiltration and metastasis occur. They stress that they should be regarded as benign tumours and treated accordingly. *S. F. Stephenson*

1051. **Involvement of Bone Marrow in Diffuse Pulmonary Disease**
A. S. WEISBERGER and R. M. DUMM. *Archives of Internal Medicine* [*Arch. intern. Med.*] **91**, 212–223, Feb., 1953. 9 figs., 5 refs.

The differential diagnosis in cases of discrete miliary opacities in the lungs is often difficult, especially between such diseases as miliary tuberculosis, pneumoconiosis, sarcoidosis, fungus disease, and metastatic carcinoma. The authors, working at Western Reserve University, Cleveland, Ohio, have studied the diagnostic value in these cases of examination of the sternal bone marrow, the results of such examination in 24 patients with diffusely distributed pulmonary lesions being compared with those obtained in 25 cases of advanced pulmonary tuberculosis.

Sections were prepared from the bone marrow and examined histologically by the method of Weisberger and Heinle (*Amer. J. med. Sci.*, 1948, **215**, 170; *Abstracts of*

World Medicine, 1948, **4**, 257). Routine bacteriological examination was carried out in all cases and, wherever possible, the diagnosis was confirmed by other means. Biopsy of lymph nodes, skin, liver, or lung was performed when indicated.

In 9 of the 24 cases of diffuse discrete miliary opacities pathological lesions were observed in the marrow; in 8 cases they were granulomatous. Three of the 9 patients had miliary tuberculosis (previously undiagnosed in 2), 2 had sarcoidosis, 2 had histoplasmosis, and one had amyloidosis. The condition in the ninth patient remained undiagnosed. The bone marrow was normal in the remaining 15 cases, though several of the patients were later found to have disease limited to the lungs. No lesions were observed in the bone marrow in 25 patients with advanced pulmonary tuberculosis, indicating that extensive pulmonary disease is not necessarily associated with dissemination.

It is concluded that histological examination of the bone marrow may be helpful in the differential diagnosis of cases showing discrete pulmonary opacities, especially if granulomatous disease is suspected.

R. J. Matthews

1052. **Studies in Thoracography with the Oscillograph of Gesenius and Keller.** (Thorakographische Studien mit dem Oszillographen nach Gesenius und Keller)
G. HILDEBRANDT and G. HILDEBRANDT-EVERS. *Zeitschrift für die gesamte experimentelle Medizin* [*Z. ges. exp. Med.*] **120**, 244–270, March 12, 1953. 15 figs., 19 refs.

Using modified sphygmomanometer cuffs, the authors recorded the range of respiratory movement in the thorax and abdomen simultaneously, both in the resting state and in maximum forced respiration. The records are analysed in great detail, emphasis being placed on the form of the tracings obtained. Included among the 110 subjects were 10 patients " with emphysema " [but the criteria on which this diagnosis was based are not stated]. The main conclusions reached are in accord with current physiological teaching. It is suggested that such records, to yield their full value, must be analysed qualitatively (that is, with regard to the shape of the tracings) as well as quantitatively. *P. Mestitz*

1053. **Cystic Malformation of the Lower Lobe of the Lung Associated with an Anomalous Artery Arising from the Aorta.** (Malformazione cistica dei lobi polmonari inferiori con vaso anomalo di origine aortica)
A. DE GASPERIS and E. DE NICOLAI. *Ospedale maggiore* [*Osped. maggiore*] **41**, 59–88, Feb., 1953. 41 figs., 34 refs.

The authors review the literature dealing with the combination of cystic disease and anomalous arterial supply in the lung, a condition which has been termed by Pryce " intralobar bronchopulmonary sequestration ". It affects one lower lobe—the right three times as often as the left—and invariably the posterior basal segment, though other lower-lobe segments may also be involved. The arterial supply comes from an anomalous vessel arising from the thoracic aorta, usually at the level of the 10th dorsal vertebra. It may occasionally be given off below the diaphragm, and occasionally also the vessels are multiple. The abnormal segment consists of cysts and rudimentary bronchi which do not communicate with the main bronchial tree. Should infection occur, the case presents as one of suppurative lung disease and there are no clinical features to distinguish it from an ordinary lung abscess or from bronchiectasis. It is important for the surgeon to be aware of this syndrome, since the anomalous artery may cause troublesome haemorrhage unless identified during lobectomy. The vessel usually enters the inferior surface of the lobe immediately behind the pulmonary ligament, and careful dissection of mediastinal adhesions is necessary.

The authors describe 4 personal cases, in 2 of which the diagnosis was made preoperatively by angiocardiography. This procedure was suggested in one case by the visualization of the abnormal artery in a tomographic film of the cystic area. In the second case angiography was performed after a bronchogram had failed to demonstrate the usual lower-lobe bronchi. In all 4 cases the venous drainage was into an inferior pulmonary vein, but drainage into the azygos or hemiazygos veins has also been reported. In Pryce's series the condition was encountered in 1·8% of 336 lobectomies, while the authors' 4 cases occurred among a total of 246 lobectomies, an incidence of 1·6%. *D. Weitzman*

1054. **Pseudo-syphilitic (Wassermann-positive) Virus Pneumonia.** (Die pseudo-luische (Wassermann-positive) Viruspneumonie)
H. HERZOG and W. PULVER. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 227–234, March 7, 1953. 8 figs., 38 refs.

Between 1940 and 1952 the authors encountered 37 patients with pneumonia in whom the result of the Wassermann reaction was transiently positive. All but 3 of the patients had fever lasting 7 to 10 days, the illness beginning in most cases with general symptoms rather than those of respiratory-tract infection. In 2 cases there were no symptoms at all, while in 15 there were signs of diffuse bronchitis, in 16 of pneumonia, and in the remaining 4 cases there were no abnormal signs in the lungs. The radiographic abnormalities consisted of ill-defined areas of mottling of various sizes, which usually disappeared in 3 to 5 weeks; in 4 cases the hilar shadow was enlarged. The positive Wassermann reaction was usually obtained 3 to 4 weeks after the radiographic abnormalities had cleared up. The presence of cold agglutinins was not demonstrated. There were no abnormal physical signs in the nervous system, but of 15 cases in which lumbar puncture was performed, in 3 some abnormality was found in the cerebrospinal fluid. The authors believe that in these cases the pneumonia was due to a virus. Similar cases have previously been reported as " pseudo-luetic perihilar bronchopneumonia " and " Wassermann-positive lung infiltrations ".

[The cases described in this paper seem to differ from other cases of pneumonia only in having a transiently positive Wassermann reaction, but this has been recorded in many diverse febrile illnesses. There is no convincing

evidence that the condition was due to a virus. To describe it as a new disease entity hardly seems justified, and may be misleading.] *J. R. Bignall*

1055. **The Intrabronchial Use of Streptokinase and Streptodornase in the Treatment of Slowly Resolving Pneumonia**
J. M. MILLER, J. A. SURMONTE, and P. H. LONG. *Diseases of the Chest* [*Dis. Chest*] **23**, 149–153, Feb., 1953. 4 figs., 11 refs.

From the Veterans Administration Hospital, Fort Howard, Maryland, the intrabronchial use of streptokinase and streptodornase in 2 cases of slowly resolving pneumonia is described. Sputum examination excluded tuberculous infection, and bronchoscopy excluded an underlying neoplasm. After as much pus as possible had been aspirated bronchoscopically and the patient had been placed so that the diseased area was dependent, a catheter was passed into the bronchus, and through this was introduced 150,000 units of streptokinase and 50,000 units of streptodornase dissolved in 10 ml. of sterile physiological saline. The bronchoscope and catheter were withdrawn and the patient requested to maintain the position for 4 hours if possible. Subsequent therapy was given through a catheter passed into the bronchial tree, and postural drainage was performed 4 times a day. In both cases the results were excellent. *I. Ansell*

1056. **The Anatomy and Radiology of Hydatid Cyst of the Lung.** (Aspects anatomo-radiologiques du kyste hydatique du poumon)
J. HOUËL and R. DUMAZER. *Journal français de médecine et chirurgie thoraciques* [*J. franç. Méd. Chir. thorac.*] **7**, 17–32, 1953. 17 figs.

From their experience of thoracotomy in 200 cases of hydatid cyst of the lung, carried out at the Centre for Thoracic Surgery, Algiers, the authors attempt to correlate the radiological appearances with the anatomical findings during operation. As expected, the radiological picture varied with the different phases in the evolution of the hydatid cyst. The authors found that the radiograph was especially characteristic during the following evolutive stages of the parasite: (1) unruptured hydatid cyst; (2) " diseased " hydatid cyst, the stage occurring immediately before rupture, when there is a fall in the intracystic pressure; (3) the rare stage of complete evacuation; (4) retention of the membrane; this acts as a foreign body, and is liable to produce many different radiological patterns varying from a dry tension cavity to frank suppuration. *A. I. Suchett-Kaye*

1057. **The Incidence of Cancer of the Lung in Coal Miners in England and Wales**
E. L. KENNAWAY and N. M. KENNAWAY. *British Journal of Cancer* [*Brit. J. Cancer*] **7**, 10–18, March, 1953. 4 figs., 9 refs.

The incidence of cancer of the lung in coal miners is less than that in the general population, and is similar to that in agricultural workers. Some possible reasons for these differences are discussed.

In the last 30 years the mortality from cancer of the lung has increased in coal miners in the same way as in the general population; in view of the peculiarities of the miner's life, this fact calls for further inquiry.

The incidence of cancer of the lung differs: (*a*) in face-workers and in other coal miners; and (*b*) in the various coalfields of England and Wales. It is low in the South Wales coalfield, where pneumokoniosis is most prevalent.—[Authors' summary.]

1058. **A Comparative Study of Ventilation and Circulation in Bronchopulmonary Cancer.** (Étude comparée de la ventilation et de la circulation dans les cancers bronchopulmonaires)
R. KOURILSKY, D. BRILLE, M. MARCHAL, and C. HATZFELD. *Journal français de médecine et chirurgie thoraciques* [*J. franç. Méd. Chir. thorac.*] **7**, 1–17, 1953. 10 figs.

In this communication the authors deal mainly with special radiological procedures designed to study the alterations in the pulmonary ventilation and circulation brought about by the presence of bronchial carcinoma. It is considered that the mapping-out of such areas of altered ventilatory and circulatory function of the affected lung is of some diagnostic and prognostic value, and is especially helpful to the thoracic surgeon when lobectomy is contemplated. *A. I. Suchett-Kaye*

1059. **Cancer of the Lung in Physicians**
E. L. WYNDER and J. CORNFIELD. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 441–444, March 12, 1953. 1 fig., 13 refs.

The replies to a questionary sent to relatives of 118 doctors dying from pulmonary carcinoma and of 214 doctors dying from carcinoma other than of the respiratory tract were analysed at the Memorial Center for Cancer, New York City, and the National Cancer Institute, Bethesda, Maryland, the object being to determine the association between tobacco smoking and carcinoma of the lung. Information was sought concerning the doctor's smoking habits and the extent to which he had been exposed to irritant dust or fumes in work or hobbies outside his professional duties. Replies were received concerning 63 of the doctors in the first group and 133 in the control group. The age distribution within the two groups was not identical, but when this was taken into account it was found that 4% of doctors in the former group smoked an average of less than one cigarette a day over the previous 20 years compared with 21% of those in the control group; the percentages smoking an average of 35 or more cigarettes a day in the two groups were 34 and 13 respectively. On the assumption that the collected information could be applied to all doctors who died from carcinoma of the lung and from carcinoma generally, mortality rates for lung carcinoma were estimated and found to be in close agreement with those estimated on similar assumptions by other workers in Britain and the U.S.A. No evidence of association of carcinoma of the lung with any other respiratory irritant was found, nor was there any association with residence in large towns. *R. Doll*

Otorhinolaryngology

1060. **Combined Oral Penicillin and Sulphadimidine in Acute Middle-ear Infections**
D. WHEATLEY. *British Medical Journal* [*Brit. med. J.*] 1, 806–808, April 11, 1953. 35 refs.

The synergism of penicillin and sulphonamides has been repeatedly demonstrated in the laboratory. In the present paper the author describes the clinical use of sulphadimidine with penicillin in 93 cases of acute middle-ear infection. The drugs were given together by mouth at 8-hourly intervals, adults receiving 1 g. of sulphadimidine and 0·375 g. (600,000 units) of penicillin, and children proportionately smaller doses. In 4 mild cases (with little constitutional disturbance but inflamed and bulging tympanic membranes) and in 28 severe cases (in which there was much pyrexia and pain or perforation of the tympanic membrane) the condition cleared up, though there was recurrence in one case within 3 months. Of 7 patients given a sulphonamide alone, 3 had a recurrence of the infection within 3 months. In 25 cases in which penicillin was given by injection (with or without a sulphonamide) the results were no better than in those in which penicillin and sulphadimidine were given by mouth. The remaining 29 patients received penicillin alone by mouth. About three-quarters of the patients were followed up for periods of one to 3 years; in none was there any residual hearing defect, as measured by ability to hear the whispered voice at 15 feet (4·6 m.) with the affected ear alone.

In the author's view the results indicate that penicillin by mouth is no less effective than penicillin by injection.

Norman W. MacKeith

1061. **Hearing Losses after Experimental Lesions in Basal Coil of Cochlea**
H. F. SCHUKNECHT and S. SUTTON. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **57**, 129–142, Feb., 1953. 8 figs., 26 refs.

It is recognized that the sound spectrum has spatial representation in the cochlea, the low frequencies at the apex and the high frequencies in the basal turn, but the effects of frequency and intensity on location and spread of sensory excitation in the cochlea are not fully understood.

Experiments with cats were performed at the University of Chicago to determine the effect on auditory function of injury to the cochlea, one inner ear being destroyed and the animal conditioned to respond to pure-tone stimuli in the other ear. The surviving ear was then damaged by pushing a needle through the round window into the selected region of the basilar membrane or the spiral lamina. Histological examination post mortem showed middle-ear damage in only one of the 8 cats used; this was also the only animal in which there was any evidence of low-tone loss. In all cases the basilar membrane was intact, but the spiral lamina was penetrated, so that both nerve fibres and Corti's organ were injured, except in one case where the spiral ganglion was damaged without injury to the organ of Corti. Audiograms showed that in cats the points of maximum excitation for frequencies from 2,000 to 14,000 cycles per second are arranged in an orderly manner in an area from 5 to 13·5 mm. from the basal end of the cochlea. Control experiments were made with apical injuries, and it was shown that with increasing intensity the spread of the excitatory process is less for high than for low frequencies. Usually it was found that lesions of the organ of Corti, especially of the hair cells, were more widespread than those in the spiral ganglion. The outer hair cells suffer more than the inner, and all hair cells disappear before the supporting cells. Furthermore, these and other experiments appear to show that there may be severe degeneration of the spiral ganglion in the presence of a normal organ of Corti.

F. W. Watkyn-Thomas

1062. **Speech Audiometry**
T. E. WALSH. *Journal of Laryngology and Otology* [*J. Laryng.*] **67**, 119–127, March, 1953. 5 figs., 7 refs.

1063. **Laryngofissure Approach in Surgical Treatment of Bilateral Abductor Paralysis**
A. A. SCHEER. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **57**, 173–181, Feb., 1953. 8 figs., 7 refs.

The object of surgical treatment of bilateral abductor paralysis is to establish an adequate airway without sacrificing the speaking voice. The first difficulty encountered with the methods in general use is to estimate the size of the glottic "chink" which will be left after the operation. If the space is wider than 6 mm. the voice will suffer, but a space of 3 to 4 mm. is needed for an adequate airway. Once the vocal cord is fixed back no further adjustment can be made, and it is not possible to guarantee that there will be no secondary contraction due to later scarring, for whatever scarring occurs will certainly alter the position of the cord. For these reasons the present author prefers a two-incision operation, starting with laryngofissure. Tracheotomy, if it has not already been performed (as it nearly always has), is now carried out. The larynx is opened and a stainless steel suture inserted through the cord and drawn through the thyroid cartilage by a second external incision, leaving the free ends of the suture in this second wound. The arytenoid is then dissected out and the mucosa sutured over the space left. The steel suture is tightened to the required degree under direct vision and tied down on the thyroid cartilage, and both wounds are closed.

The author has performed this operation in two stages, but does not regard this as a practical procedure.

F. W. Watkyn-Thomas

Urogenital System

1064. **A Clinical and Pathological Study of Carcinoma of the Urinary Bladder**

J. H. HEJTMANCIK and J. H. CHILDERS. *Journal of Urology* [*J. Urol. (Baltimore)*] **69**, 377–389, March, 1953. 15 refs.

An attempt was made to correlate the clinical, histological, and microscopical grading of bladder tumours with treatment and prognosis in 96 consecutive, unselected cases of malignant neoplasm of the urinary bladder at John Sealy Hospital, Galveston, Texas. The clinical classification of the tumours was as follows: Grade I, confined to the mucosa and submucosa; Grade II, early invasion of the muscular wall; Grade III, invasion of more than one-half of the muscular wall but still confined to the bladder; and Grade IV, invasion beyond the bladder wall, and/or metastases. Microscopically, the tumours were graded A, B, C, and D, the same criteria being used as for the clinical classification. The histological grading was based on the cellular anaplasia thus: Grade 1, cells uniform with infrequent mitoses and absence of invasion; Grade 2, cells thrown into sheets which varied from 7 to 16 layers, with an occasional mitotic figure; Grades 3 and 4, more anaplastic lesions, Grade 4 being the most undifferentiated.

In the clinically Grade-I tumours (17) there was little discrepancy in the three classifications, there being recurrences in only one case. The tumours were confined to the lateral wall in 10 cases, to the trigone in 6, and to the bladder neck in one, but there was no apparent relation between the site of the tumour and the degree of malignancy. The best treatment in such cases, in the authors' view, is transurethral resection.

In the clinically Grade-II tumours (34) there was considerable discrepancy [it is well known that these are the most difficult tumours to assess clinically]. Thus in 16 cases it was impossible to determine whether the muscle was invaded and in another 3 the actual depth could not be gauged. Microscopically, 5 tumours showed Grade-A, 6 Grade-B, 3 Grade-C, and one Grade-D invasion. In 3 cases the growth was classified as squamous-cell carcinoma and in 31 as transitional-cell carcinoma. The site of the tumour was the lateral wall in 17 cases, the trigone in 8, the vault in 3, the bladder neck in 5, and the posterior wall in one. The most satisfactory results of treatment in Grade-II tumours were obtained with suprapubic cystostomy and electrocoagulation, though transurethral resection was fairly successful; the results of partial cystectomy were considered " questionable ".

In Grade-III tumours (26) there was considerable agreement; only in 3 cases was it impossible to determine whether muscle invasion had occurred, although in another 4 cases the depth of the invasion could not be ascertained. The tumour originated in the trigone in 6 cases, the bladder neck in 2, the lateral wall in 6, the posterior wall in 3, and the vault in 3; in 6 cases the tumour was so extensive that the site of origin could not be determined. Partial cystectomy appeared to give better results than total cystectomy, except in patients in the younger age group with a highly invasive tumour of the bladder neck or the trigone.

There was little difficulty in assessing Grade-IV tumours; of the 19 patients 17 died, the survival time being, on the average, 14 years short of the expected span of life. *S. M. Vassallo*

1065. **Electrolyte Metabolism during Rice Diet. II. Serum Electrolytes in Patients with Severe Primary or Secondary Renal Disease**

E. PESCHEL and R. L. PESCHEL. *Archives of Internal Medicine* [*Arch. intern. Med.*] **91**, 296–303, March, 1953. 2 figs., 14 refs.

In an investigation at Duke University School of Medicine, Durham, North Carolina, the effect on the serum electrolyte level of strict rice diet administered for a long period was studied in 80 patients, aged between 4 and 64 years, with severe primary or secondary renal disease (chronic glomerular nephritis, 33; Kimmelstiel–Wilson syndrome, 5; chronic pyelonephritis, 4; polycystic kidney, 4; arteriolo-nephrosclerosis, 24; malignant hypertension, 10). Proteinuria was present in all 80 patients, the non-protein nitrogen (N.P.N.) level in the blood being above 40 mg. per 100 ml. in 67, and the phenolsulphonphthalein (P.S.P.) excretion in 2 hours exceeding 40% in only 10. Even patients with severe renal failure maintained a normal serum electrolyte balance for remarkably longer periods than seemed possible on theoretical considerations.

The serum N.P.N. level proved less useful as a guide to the patient's ability to maintain the serum electrolyte balance than the P.S.P. excretion. The authors were able to treat 36 patients with an average N.P.N. level of 61 mg. per 100 ml. and an average P.S.P. excretion of 29% in 2 hours as though they had a completely normal renal regulatory capacity. It was not until these patients had been receiving the rice diet for 4 months that serum electrolyte determinations indicated that a modification of the diet was necessary, 2 to 4 mEq. of sodium chloride per day being all that was required to restore the electrolyte equilibrium. In 12 patients major electrolyte disturbances developed later after further periods on the rice diet varying from 2 to 17 months, necessitating further adjustment. In another group of 44 patients major electrolyte disturbances developed before the lapse of 4 months; the P.S.P. excretion in these cases had been 28% or less in 2-hour tests. Some patients with cardiac oedema or in the nephrotic stage of chronic glomerular nephritis were apparently using electrolytes from fluid stored in the tissues, and were able to replenish their serum electrolyte requirements from that source while the water was excreted. *L. H. Worth*

KIDNEY AND URETER

1066. **Kidney Homotransplantation**
W. J. DEMPSTER. *British Journal of Surgery* [*Brit. J. Surg.*] **40**, 447–465, March, 1953. 16 figs., bibliography.

In this paper from the Postgraduate Medical School, London, and the Buckston Browne Research Farm, Downe, Kent, the author discusses the behaviour of autotransplanted and homotransplanted kidneys in the dog and analyses the results of 85 experiments in which a kidney was transplanted into the neck.

In 5% of cases the kidney is anuric from the start, but the cause of this is obscure. In the remainder the kidney functions as a normal organ for 2 to 12 days. The homotransplanted kidney is unable to concentrate salt as well as the autotransplanted organ. The initial stage in disintegration consists in a plasma-cell infiltration, which can be interpreted either as a local reaction against the transplant or as an attempt at antibody formation against the host; the latter is considered the more likely. It is tentatively suggested that the origin of the plasma cells is the renal vascular endothelium. A possible cause of the arrest of function is a generalized vascular spasm, reflected particularly in the tuft capillaries. Nephro-arteriograms show reduced cortical circulation.

The author believes that the local tissues of the host take no part in rejecting the homotransplant, and he concludes that the process must be mediated by a humoral mechanism. His findings do not support the theories of Loeb, who maintained that a local tissue immunity in the host was responsible; but he points out that Loeb's experiments were carried out with implanted tissue and not with transplanted organs. *K. Whittle Martin*

1067. **Primary Ureteral Tumors**
M. R. KEEN. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **69**, 231–242, Feb., 1953. 5 figs., 27 refs.

The author describes 6 cases of primary ureteric tumour seen in private practice at Huntington, N.Y., five of which were malignant. The malignant cases occurred in patients aged 47 to 61 years; 3 were males, of whom one, aged 59, presented with metastases in the lungs, and a second, aged 47, died from vesical recurrence after nephrectomy and ureterectomy. The other man and two women are alive after operation, although the man had malignant tumours of both the bladder and the ureter. Removal of the kidney, ureter, and cuff of the bladder is recommended. The benign case, in a woman of 55, was similarly treated.

In all the cases except one the first symptom was haematuria, sometimes not associated with pain. In the exceptional case there was colic with frequency and urgency of micturition, but no haematuria. The insidious nature of the symptoms is stressed. The results of radiography may be confusing, the tumours may be multiple, and the symptoms in women may be confused with a gynaecological lesion.

The pathogenesis of these tumours is fully discussed, and the cell-nest theory of their origin is not substantiated. Reference is made to a number of the 245 primary malignant tumours (some bilateral) and 75 benign tumours of the ureter described in the literature. It is the author's impression that the diagnosis is now being more frequently made and confirmed; his own cases gave an incidence, based on the total number of urological cases seen since 1939, of about 1 in 1,300.

W. Skyrme Rees

1068. **Primary Ureteral Tumors with a Review of the Literature since 1943**
F. L. SENGER and C. A. FUREY. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **69**, 243–258, Feb., 1953. 6 figs., bibliography.

A review of 130 cases of primary ureteric tumours (31 benign) is presented from the Long Island College Hospital, Brooklyn, N.Y., together with an account of 2 cases successfully treated by the authors by nephro-ureterectomy and partial cystectomy. Although recently more frequently diagnosed, these tumours are still commonly missed. The first preoperative diagnosis is attributed to Albarron in 1902. By 1934 a further 60 cases were confirmed, and this had risen to 180 by 1943. There are now 310 cases in the literature. Fagerstrom (*J. Urol.* (*Baltimore*), 1948, **59**, 333) believes that the cause is local irritation from chronic infection, in sharp contrast to von Brunn's theory of a "cell-nest" origin.

Of the tumours of the urinary tract 85·5% are situated in the bladder or renal cortex, and only 8·4% are in the ureter or renal pelvis. Papillary ureteric tumours are twice as common as non-papillary; 80% of cases occur in subjects aged 50 to 70 years, and the condition is more frequent in males. The lower third of the ureter is the commonest site, the most difficult region to define by ureterograms and requiring the use of a Woodruff catheter. Haematuria and pain are present, and the presence of an abdominal mass is known (on an average) for over 18 months before diagnosis is made. On cystoscopy, the tumour is sometimes seen protruding from a ureteric orifice, and in over half the cases an obstruction to ureteric catheterization is encountered. Retrograde pyelography gives the most important evidence, and if thoroughly carried out will usually justify exploration of the ureter at operation. Where hydro-ureter is present, even the most casual retrograde pyelography will show the lesion. Obstruction, dilatation of a ureter, and goblet-shaped filling defects are seen. Excretory pyelograms are valueless in defining the tumour, but are, of course, essential for demonstrating the presence of a good kidney on the other side, since treatment is by nephro-ureterectomy and partial cystectomy. Some benign tumours have been treated by resection of the ureter and anastomosis, but there is reason to believe that even histologically benign tumours of this sort are potentially malignant. Fulgurization alone and pre- and post-operative deep *x*-ray therapy are of doubtful value.

Three cases of survival for 25, 14, and 10 years respectively after operation have been reported elsewhere, but in this series the longest period of survival was 9 years. The bladder, ureter, peri-ureteric tissue, lung, bone, and brain, in that order of frequency, are the commonest

sites of recurrence, and carcinomatosis is the most frequent cause of death. In 24 cases which the authors followed up the average survival time was 21 months. The figures indicate that the best outlook follows the more radical surgical procedures. Staining of the urinary deposit by the Papanicolaou method may facilitate earlier diagnosis.

[It must be evident, however, that cases of haematuria cannot be said to be fully investigated until ureterograms defining the whole length of both ureters are available.]

W. Skyrme Rees

1069. **Glomerulonephritis as a Complication of the Schönlein–Henoch Syndrome**

L. M. Levitt and B. Burbank. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 530–536, March 26, 1953. 6 figs., 19 refs.

In this report from Long Island College Hospital, New York, 5 cases of the Schönlein–Henoch syndrome complicated by glomerulonephritis are described. In 3 of the cases the evidence for this was only clinical; all 3 patients had pain in the joints and haemorrhages either into the skin or from the alimentary tract, or both, and all had albuminuria with microscopic haematuria and occasional granular casts. The blood urea level was normal in 2 cases, and in the 3rd was 48 mg. per 100 ml. Two of these patients had been treated with penicillin for respiratory infection before the appearance of the purpuric manifestations, and the 3rd had been treated with " ivyol " for dermatitis due to poison ivy. Recovery was uneventful, although microscopic haematuria persisted for some time after discharge from hospital.

The 4th case occurred in a man who was admitted with bilateral pulmonary tuberculosis and who received penicillin for an intercurrent pharyngitis. Two days later he developed a purpuric rash, followed by gross haematuria, arthralgia, and melaena. He recovered from this but died of acute caseating tuberculous bronchopneumonia. Histological examination of sections of kidney showed degeneration of the proximal convoluted tubules, increased cellularity of the glomerular tufts, and crescent formation in Bowman's capsule. The 5th case occurred in a boy of 15, who developed epistaxis, haematemesis, and haematuria after eating strawberries. He later became hypertensive and died from uraemia. Microscopical examination of the kidneys showed partial fibrosis of the glomerular tufts with fibrinoid changes in the intima, and varying degrees of epithelial atrophy in the cortical tubules. Other organs showed evidence of generalized arteriolitis.

Discussing these cases, the authors consider that the Schönlein–Henoch syndrome represents an allergic response to a wide variety of antigens. Pathologically, there is increased capillary permeability which is usually a temporary change. In their 5 cases they point out that the changes extended to the renal capillaries, and that in the last case the change developed into a fulminating glomerulonephritis with lesions in other organs, resembling in some respects the lesions seen in disseminated lupus erythematosis and in others those seen in polyarteritis.

J. Lister

PROSTATE GLAND

1070. **Inhibitory Effects of Portal Cirrhosis of Liver on Prostatic Enlargement**

H. H. Stumpf and S. L. Wilens. *Archives of Internal Medicine* [*Arch. intern. Med.*] **91**, 304–309, March, 1953. 1 fig., 21 refs.

The prostates of 333 men with cirrhosis, aged 50 years and over, and those of a similar number of controls of the same age were compared as to the degree of hypertrophy. There is a lower incidence of significant hypertrophy of the prostate in men with cirrhosis. Moreover, not only is the incidence less but the age of onset of hypertrophy in cirrhotic patients is delayed as compared with the control group. The difference is accentuated if only cases of moderate and severe hypertrophy are compared. While the exact nature of this relationship cannot be determined, it is suggested that protractedly elevated estrogen levels or other hormonal imbalance may be responsible for the lower incidence of prostatic hypertrophy in cases of portal cirrhosis of the liver.—[Authors' summary.]

1071. **The Persistence of Urinary Infection following Prostatectomy**

M. Caine. *British Journal of Urology* [*Brit. J. Urol.*] **25**, 9–19, March, 1953. 14 figs., 8 refs.

In a follow-up study carried out at St. Paul's and St. Peter's Hospitals, London, urinary infection was found to be present 1 to 5 years after prostatectomy in 269 of 518 patients (52%). Of these patients, 120 (23·3%) passed urine turbulent with pus, while in 149 (28·8%) the urine gave positive cultures, mainly of *Bacterium coli*; in the remaining 48% the urine was sterile. This high incidence of persistent infection of the urine was the more surprising when it was found that 30% of the patients had sterile urine before prostatectomy.

The fibrous and calculous varieties of prostatic lesion were found to be those most usually associated with persistent postoperative urinary infection. There was a significantly higher incidence of infection after transurethral prostatectomy by electrotome than in those treated by " punch " resection or by retropubic and vesico-capsular prostatectomy. This was true even taking into account the fact that transurethral resection is more commonly employed for the fibrous prostate, and is attributed to the effect of electrocoagulation of the tissues. The incidence of infection was also significantly higher after the Freyer type of prostatectomy and two-stage operations, in which the bladder is drained suprapubically, than the Millin, Harris, or vesico-capsular techniques, in which the bladder is closed.

Urinary stasis was found to be the chief factor responsible for the persistence of infection. The main causes of the stasis were hypertrophy of residual prostatic tissue (22 cases), bladder-neck obstructions (18), vesical diverticula (17), hypertrophy of the trigone (7), calculi (7), urethral stricture (7), and pyonephrosis (3); the kidney later responsible for the persistent infection could be detected in the preoperative pyelograms in 2 of the 3

cases. Apart from urinary stasis, irregular prostatic cavities which had contracted incompletely after prostatic enucleation and in which there were small pockets were important causes of persistent infection. Such irregular, infected prostatic urethrae were most commonly associated with prostatectomy involving suprapubic drainage, and the condition is attributed to pus lying in the prostatic cavity causing faulty healing of the prostatic bed in the early postoperative days. In support of this theory is the fact that when a catheter is passed in the postoperative management of a Freyer's prostatectomy a quantity of thick pus often escapes before any urine. It is possible that such a collection of pus could be prevented by using a fine urethral tube for irrigation, as is sometimes done in this operation. It is also possible for pus to collect in the prostatic cavity when the bladder is drained by a Foley's catheter unless extra holes are provided between the bag and stem of the catheter.

Some urinary infection after prostatectomy is almost invariable, but it normally clears after 2 to 4 months. The author suggests that some of the main causes could be prevented: for example, if perineal urethrostomy were substituted for catheter drainage, urethral strictures might not arise; if preoperative cystoscopy were performed diverticula would be found and could be treated; and suprapubic drainage should be avoided whenever possible. Urethroscopy and cysto-urethrograms are invaluable methods of investigation in discovering the causes of persistently infected urine following prostatectomies. Several such urethrograms are illustrated in the text.

Charles P. Nicholas

1072. **An Evaluation of Endocrine Control Therapy followed by Radical Perineal Prostatectomy on Selected Cases of Advanced Prostatic Carcinoma**

W. W. Scott. *Cancer* [*Cancer* (*N.Y.*)] **6**, 248–265, March, 1953. 21 figs., 9 refs.

In this paper from the University of Rochester, Rochester, New York, the author sets out to show that there is an encouraging number of patients with carcinoma of the prostate who will benefit from endocrine therapy combined with radical perineal prostatectomy. The most suitable cases are those with advanced carcinoma of the prostate, without metastases, in which the extension of the growth beyond the confines of the prostate, while not marked, is too great to permit complete extirpation by radical surgery at the time of first examination. If the patient's response to hormone therapy is such that digital examination at the time of maximum regression suggests that complete extirpation of the lesion is possible, radical perineal prostatectomy offers a chance of cure or, failing this, prolongs life, with freedom from distressing symptoms. Of 28 cases treated on these lines, 21, in which the follow-up period was at least 3 years, are described in detail, the remaining 7 being too recent for adequate assessment of results. In 18 of the cases carcinoma was confirmed at biopsy examination either before or shortly after the start of endocrine therapy.

The results of treatment were striking. One patient was under observation for as long as 118 months from the start of endocrine therapy, the average being 65·3 months. Three patients died within 3 years, one from coronary thrombosis, one from prostatic carcinoma 14 months after the start of treatment, and one from metastases 28 months after beginning treatment. The percentage of patients surviving at 6-monthly intervals from the start of treatment to the end of the 3-year period was 100, 100, 90·5, 90·5, 85·7, and 85·7. These figures are compared with those obtained by Nesbit and Plumb in 273 cases without metastases treated before the introduction of endocrine therapy, the percentage of patients surviving at 6-monthly intervals in that series being 72, 54, 39, 37, 28, and 22 (*Surgery*, 1946, **20**, 263; *Abstracts of World Surgery*, 1947, **1**, 92). The present author's results also compare favourably with those obtained by other workers in the treatment of prostatic carcinoma by administration of stilboestrol, by castration alone, or by a combination of these two. [Encouraging as the author's figures are, it must be remembered that the field of usefulness of this method of treatment is very restricted.]

The author considers that whatever method is employed for radical prostatectomy, all patients undergoing this operation should continue a routine course of oestrogen therapy for a considerable time afterwards.

D. P. McDonald

1073. **The Response of Prostatic Carcinoma to Oestrogen Treatment**

J. D. Fergusson and L. M. Franks. *British Journal of Surgery* [*Brit. J. Surg.*] **40**, 422–428, March, 1953. 10 figs., 7 refs.

The response of prostatic carcinoma to oestrogen therapy was studied in 82 specimens removed at biopsy or necropsy from 33 patients at the Central Middlesex Hospital, London.

It is pointed out that histological changes due to administration of oestrogens may appear very shortly after start of treatment, the first being the appearance of small intracytoplasmic basal vacuoles which coalesce, forming a large swollen " balloon " cell. The nucleus is pushed to one side and becomes hyperchromatic and later pyknotic.

The specimens in the authors' series were graded, but the grading was of little value in assessing prognosis or the likely response to treatment. The most important feature was that even in specimens showing a marked response histologically to oestrogen therapy there were always surviving tumour cells; in no case were all the tumour cells destroyed. Response of the breast to oestrogens was often associated with a good clinical response.

The authors consider that the optimum dosage of oestrogens has yet to be determined and that this may well be higher than that generally given. In some cases a tumour which had apparently become resistant responded markedly when the dose of the oestrogen was increased.

K. Whittle Martin

1074. **Bladder Tumor Recurrence in the Urethra: a Warning**

J. H. Kiefer. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **69**, 652–656, May, 1953. 6 refs.

Endocrinology

1075. **The Effect of ACTH and Cortisone on Cerebral Blood Flow and Metabolism**
W. SENSENBACH, L. MADISON, and L. OCHS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **32**, 372–380, April, 1953. 13 refs.

Measurements of cerebral circulatory and metabolic functions were made in a series of patients before, during, and after treatment with cortisone and ACTH, and in 2 patients with Cushing's syndrome. Parallel increases in the mean arterial blood pressure [MABP] and cerebral vascular resistance [CVR] occurred in both the cortisone and ACTH treated patients. The mean cerebral blood flow [CBF] was unchanged. The results are interpreted to mean that the cerebral circulation shares equally in an increase in general peripheral vascular resistance. ACTH and cortisone do not appear to exert a specific, local effect upon cerebral blood vessels. Similar changes in the cerebral circulation, that is, parallel increases in MABP and in CVR, with normal CBF were found in two subjects with Cushing's syndrome. Significant changes in the mean cerebral utilization of oxygen and glucose did not occur during the administration of cortisone or ACTH. Cerebral oxygen and glucose utilization were normal in patients with Cushing's syndrome.

These studies provide no explanation for the mental changes that occurred during the administration of cortisone and ACTH.—[From the authors' summary.]

PITUITARY GLAND

1076. **Effects of Anterior Pituitary Extracts and of Growth Hormone Preparations on the Islets of Langerhans and the Pancreas**
B. KINASH, I. MACDOUGALL, M. A. EVANS, F. E. BRYANS, and R. E. HAIST. *Diabetes* [*Diabetes*] **2**, 112–121, March–April, 1953. 2 figs., 13 refs.

Anselmino *et al.* (*Klin. Wschr.*, 1933, **12**, 1245) first reported that injection of anterior pituitary extract in rats led to an increase in pancreatic islet tissue. Other workers have made similar observations in both intact and hypophysectomized animals. In the latter the apparent increase in islet volume may arise because a marked reduction in the acinar tissue of the pancreas follows hypophysectomy and so leads to a relative increase in the proportion of islet tissue.

The present authors, at the University of Toronto, have investigated the effect on islet weight of injecting anterior pituitary extract and purified growth hormone into both intact and hypophysectomized rats. The injection of crude saline and globulin extracts of the anterior pituitary into intact rats increased the islet weight compared with control animals, but the body weight also increased so that the islet weight per 100 g. body weight was not much altered. In hypophysectomized rats the daily injection of a saline extract of anterior pituitary caused growth of islet tissue, although it did not completely restore the loss of pancreatic weight which followed hypophysectomy.

The injection of growth hormone into intact animals caused a significant rise in islet weight above that of the controls. In hypophysectomized animals it caused an increase in islet weight above the level in hypophysectomized, untreated animals, but the body weight also increased so that there was no increase in islet weight per 100 g. body weight in this group.

It is pointed out that the means by which the pituitary stimulates growth of the islets of Langerhans in intact and hypophysectomized rats has not been clearly demonstrated. Atrophy of pancreatic islets does not occur to any extent within a period of weeks of hypophysectomy, so that it is not suggested that there is a pituitary pancreatrophic effect in the same sense as there are thyrotrophic and adrenocorticotrophic effects.

The authors suggest that the increase in islet-cell tissue following injection of pituitary extract and growth hormone, at any rate in the intact animals, may represent a compensatory response to the increased requirements of insulin which follow from the diabetogenic effects of these preparations. *J. Lister*

1077. **Isolation of Pituitary Antidiuretic Peptide and Similar Urinary Peptide by Paper Chromatography**
G. C. ARNEIL and H. E. C. WILSON. *Lancet* [*Lancet*] **1**, 568–570, March 21, 1953. 3 figs., 8 refs.

In 1948 Dent (*Biochem. J.*, **43**, 169) reported the detection of an unusual peptide in the urine of patients with nephrosis. The present authors, working at the Royal Hospital for Sick Children, Glasgow, have on numerous occasions confirmed this finding, and have also obtained a similar peptide from the urine of patients with oedema due to other causes, such as pre-eclamptic toxaemia and polyarteritis nodosa, and of patients who had sustained trauma such as burns, scalds, or fractures, or recently undergone surgical operation. Hydrolysis of the peptide showed that it contained twelve amino-acids.

The antidiuretic activity of the peptide was investigated because an excessive antidiuretic activity had been reported to be present in the blood of patients with nephrosis. Peptide specimens from 7 patients, when injected subcutaneously into rats on 22 occasions, elicited a well-marked antidiuretic response in only 3 instances. In 2 normal volunteers (non-smokers) in whom diuresis was induced by drinking a litre of warm water, the smoking of a cigarette produced a good antidiuretic response; no peptide was detected in the urine passed by either subject before smoking, but antidiuretic activity and peptide were present in the urine after smoking.

Eight commercial extracts of posterior pituitary gland were then examined by paper chromatography, and a

peptide having strong antidiuretic activity was isolated. This fraction contained the same 12 amino-acids as the urinary peptide and the two substances behaved similarly when tested by chromatography, electrophoresis, and hydrolysis. However, the antidiuretic effect of the pituitary peptide fraction was much more consistent than that of the urinary peptide fraction.

The authors suggest that at least some part of the peptide excreted in the urine in the group of diseases characterized by oliguria and oedema is the altered form in which the antidiuretic peptide of the posterior lobe of the pituitary gland is excreted. An imbalance of hormones, together with an excess of the pituitary peptide, may be concerned in some way with the production and course of such diseases. *M. J. H. Smith*

1078. **The Arterial Blood Supply of the Human Hypophysis Cerebri**
E. M. McCONNELL. *Anatomical Record* [*Anat. Rec.*] **115**, 175–203, Feb., 1953. 11 figs., 29 refs.

Three methods have been employed in the study of the blood supply of the human hypophysis: (*a*) serial sections of uninjected glands with their associated structures; (*b*) injection of the hypophyseal arteries via the internal carotid arteries within the neck, followed by examination of the vessels to the gland and the stalk; (*c*) selective injection of the superior and inferior hypophyseal arteries using various injection masses.

These investigations lead to the following conclusions: (*a*) The anterior and posterior lobes have a relatively independent blood supply. The anterior lobe is supplied by the superior hypophyseal arteries, which arise on each side from the internal carotid artery immediately after this vessel has pierced the dura mater. The posterior lobe is supplied by the inferior hypophyseal artery, which arises on each side from the internal carotid artery as this vessel lies within the cavernous sinus. (*b*) The blood supply of the anterior lobe passes first through three different types of capillaries in the stalk, and is then collected again by portal sinuses which pass down the stalk to the anterior lobe. (*c*) There is an overlap of distribution of the superior and inferior hypophyseal arteries in the region of the stalk, in the small wedge of the anterior lobe which lies in front of the intraglandular stalk, and in a few small subcapsular areas of the anterior lobe.—[Author's summary.]

THYROID GLAND

1079. **Cerebral Blood Flow and Oxygen Consumption in Hyperthyroidism before and after Treatment**
L. SOKOLOFF, R. L. WECHSLER, R. MANGOLD, K. BALLS, and S. S. KETY. *Journal of Clinical Investigation* [*J. clin. Invest.*] **32**, 202–208, March, 1953. 28 refs.

The cerebral blood flow and the metabolism of the brain in hyperthyroidism were investigated at the University of Pennsylvania. In 11 hyperthyroid patients the cerebral blood flow and oxygen consumption were determined before treatment, and in 7 of these after treatment as well. Before treatment began the cerebral oxygen consumption and arterial blood pressure were normal and the cerebral blood flow was moderately raised, probably due to an associated anaemia. The level of the blood gases was normal except for the low oxygen content associated with anaemia, while the cerebral vascular resistance was low. Treatment did not effect any significant change, with the exception of a decrease in the basal metabolic rate to normal level and an increase in the cerebral respiratory quotient. It is suggested that the gross energy metabolism of the brain may be independent of the action of the thyroid hormone. *F. W. Chattaway*

1080. **Effective Half Life of Radioactive Iodine (I^{131}) in the Hyperthyroid Gland. Its Significance in the Treatment of Thyrotoxicosis**
C. E. SCHMIDT and J. NADELHAFT. *Laboratory Investigation* [*Lab. Invest.*] **2**, 133–139, March–April, 1953. 3 figs., 10 refs.

Radioactive iodine (^{131}I) was the sole agent used in the treatment of 100 hyperthyroid patients at the Presbyterian Hospital, New York, and in this paper the authors analyse the results. Measurement of the "effective half-life" in each patient—that is, the time taken for the ^{131}I in the thyroid to decrease by 50%, without correction for physical decay—indicated the rate at which radiation was delivered to the gland, a shorter effective half-life indicating that the radiation had been delivered more rapidly. Only one treatment was required by 65 of the patients and the effective half-life and dose of ^{131}I in this group were compared with those of the remaining 35 who failed to respond satisfactorily to the first dose.

The success rate was highest in patients who received a large radiation dose (measured in roentgen equivalents) in a short time, and lowest in those patients who received a low dose delivered over a long period. A further analysis of two groups of patients, each receiving the same total radiation dose, revealed that the success rate was statistically higher in the group receiving ^{131}I with a short effective half-life.

The authors conclude that the proportion of successful results is higher when the rate of irradiation is relatively rapid than when it is relatively slow. They therefore suggest that treatment should be planned to provide rapid delivery of an adequate dose. *G. Ansell*

DIABETES

1081. **Serum Lipids in Diabetic Acidosis**
L. V. D. HARRIS, M. J. ALBRINK, W. F. VAN ECK, E. B. MAN, and J. P. PETERS. *Metabolism* [*Metabolism*] **2**, 120–132, March, 1953. 2 figs., 21 refs.

In 15 diabetic patients in a state of acidosis at New Haven Hospital (Yale University School of Medicine) the serum concentrations of total and free cholesterol, total fatty acid, lipid phosphorus, and bicarbonate, and

the total blood sugar were estimated. No correlation was found between the blood sugar level or serum bicarbonate level and the degree of lipaemia. It is known that lipid levels in individual diabetic patients vary much more than in normal subjects, increases of neutral fats up to twice the upper normal limit of 6 mEq. per litre being common in a large proportion of patients. In the patients described all lipid components diminished in the course of treatment, the cholesterol concentration, which at the beginning of treatment exceeded the upper normal limit (320 mg. per 100 ml.) in 3 patients only and in one was slightly below the normal mean, being reduced, but to a considerably lesser degree than fatty acids; phospholipid levels occupied an intermediate position. The free cholesterol level fell proportionately more than the total cholesterol level, the ratio of free to total cholesterol (in normal persons between 0·24 and 0·32 to 1) exceeding the upper limit in all but 2 patients. A high ratio denotes a hepatic disorder, and in this group all patients had enlarged livers at the height of the acidosis.

The authors conclude that the metabolic disorder in diabetes interferes with the processes by which fatty acids are transformed to lipid phosphorus and cholesterol esters and attached to proteins, and thus produces the increase and change of pattern of the serum lipids. Normally these lipids originate in the intestine and reach the blood via the lymphatics; in the diabetic patient with acidosis they originate from the depots, and their presence in the serum in the free state, not combined with protein, accounts for the lactescence of the serum.

L. H. Worth

1082. **The Early Detection of Arterial Disorders of the Limbs in Diabetes.** (Le dépistage précoce des troubles artériels des membres chez les diabétiques)

A. JOUVE, J. PIERRON, and E. BOURDONCLE. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **48**, 108–116, Feb., 1953. 27 refs.

Arteriosclerotic disease remains an important cause of disability in diabetes, and early diagnosis is therefore important, although a major arterial obstruction is often the first clinical manifestation of vascular disease. The authors attribute the failure of the usual diagnostic methods in the early stages to the development of the condition in the arterioles and capillaries rather than in the arteries. Since these lesions are probably spastic at first, early treatment might prevent progression of the disease.

They attach considerable importance to the patient's morphological type, having observed that there is a tendency to the masculine type of build in diabetics of either sex (well-developed muscles and obesity of the upper half of the body), especially in the presence of arterial changes. In addition, however, they place much reliance on the fluorescein test for determining the state of the arteriolo-capillary circulation. After producing a series of histamine weals on the legs, 5 ml. of 2% fluorescein is injected into the femoral artery, and under ultraviolet light the rate of appearance of fluorescence in the weals is noted. This was found to be delayed in certain cases even when oscillometric and arteriographic studies gave apparently normal results. It is considered that fluorescein tests should be performed on all diabetics and that particular care should be taken to follow up those showing evidence of vasoconstriction.

[No adequate information is given of the results obtained or of any effective treatment which might justify the routine use of this method for early diagnosis.]

Keith Ball

1083. **Steroid Diabetes in Man. The Development of Diabetes during Treatment with Cortisone and Corticotropin**

J. J. BOOKMAN, S. R. DRACHMAN, L. E. SCHAEFER, and D. ADLERSBERG. *Diabetes* [*Diabetes*] **2**, 100–111, March–April, 1953. 3 figs., 20 refs.

The term steroid diabetes was introduced by Ingle *et al.* (*Endocrinology*, 1945, **37**, 341) to describe the diabetes induced in rats by the administration of Compounds B, E, and F and corticotrophin (ACTH). Insensitivity to insulin, a negative nitrogen balance, and a reduction in the glycosuria with fasting in the absence of insulin, were the features which distinguished this form of diabetes from pancreatic diabetes.

The present authors describe 5 cases in which glycosuria and fasting hyperglycaemia developed during treatment with ACTH and/or cortisone. Before treatment the fasting blood sugar level was normal and there was no glycosuria, although one patient was considered to be a latent diabetic because casual urine analysis 10 years before had revealed glycosuria. In all these cases the degree of hyperglycaemia and the degree of glycosuria were proportional to the dose of the hormones, and in all except one the signs of diabetes disappeared when administration of the drug ceased or the dose was reduced. The exception was the latent diabetic, who was also the only patient in whom cortisone alone precipitated hyperglycaemia. In 3 cases hyperglycaemia developed when ACTH was given after preliminary cortisone therapy, and in the remaining case hyperglycaemia was observed after administration of ACTH only.

The cases presented several of the features of the steroid diabetes of rats; in 2 there was relative resistance to insulin and in one a negative nitrogen balance. The authors stress that 4 of the 5 patients had a family history of diabetes, and suggest that it was the familial predisposition to diabetes which was responsible for the development of hyperglycaemia under the stress of hormone therapy. They further suggest that trauma, such as fractures and burns, and infections may cause similar hormonal stress and precipitate steroid diabetes in predisposed individuals. On the other hand, the possibility that ACTH and cortisone may cause an alteration in the renal reabsorption of glucose should not be overlooked.

J. Lister

1084. **Antagonism between Diabetes Mellitus and Allergic Diseases, especially Bronchial Asthma**

M. J. GUTMANN. *International Archives of Allergy and Applied Immunology* [*Int. Arch. Allergy*] **4**, 118–128, 1953. 4 figs., 38 refs.

The Rheumatic Diseases

1085. **Rheumatic Complaints in an Urban Population**
J. H. KELLGREN, J. S. LAWRENCE, and J. AITKEN-SWAN. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **12**, 5–15, March, 1953. 3 figs., 10 refs.

The incidence of " rheumatic complaints " over a 5-year period among the industrial population (48,714) of Leigh, Lancashire, was investigated, with special reference to climate and the age, history, and occupation of the subjects. A random sample was obtained by visiting every tenth house and questioning all persons over 15 normally resident there. Of 3,515 subjects interviewed, 1,407 complained of rheumatic manifestations and were seen by a doctor. ' [The statistical material in this paper cannot be abstracted, but a few of the more important findings may be mentioned.]

The over-all complaint rate of " rheumatism now "—that is, in 1949–50 when the survey was actually carried out—was 19% [surprisingly high]; during the preceding 5-year period it was 33%. The complaints were classified in broad diagnostic groups, and the age incidence, occupation of the subject, degree of disability, and extent of medical care were analysed. Of the females with rheumatoid arthritis and osteoarthritis, 38% and 50% respectively had failed to consult a doctor, a finding, in the authors' view, which strongly suggested a general belief that " the doctor can do nothing about it ". There was a significant association in males between a history of injury and the occurrence of osteoarthritis. The authors emphasize the high incidence of osteoarthritis in females and the part played by disk disorders in the causation of pain and disability. It is concluded that the findings, when compared with those of earlier workers, show a similar total incidence of complaints, but some difference in the allocation to the various diagnostic groups, which might be due to differences in diagnostic criteria and, possibly, to some difference in the types of population studied. *Harry Coke*

1086. **Contributions to the Pathogenesis of Acute Rheumatism. I. The Significance of Disturbances of Permeability.** (Beiträge zur Pathogenese des akuten Rheumatismus. I. Die Bedeutung der Permeabilitätsstörung)
H. ECKERT, J. GLEISS, and F. KÜSTER. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] **72**, 452–462, 1953. 2 figs., 22 refs.

In 1950 Frontali reported that in patients with acute rheumatism he had found an anatomical abnormality of the capillaries and an impairment of their resistance, affecting probably the whole body and persisting often for years after the acute rheumatic episode. He postulated an abnormal endothelial constitution as the basis for the tendency to rheumatic fever. In order to shed more light on this problem the authors examined the capillary resistance of 24 children with acute rheumatism at the Medical Academy, Düsseldorf. They used the method of applying negative pressure to the skin of the infraclavicular region; in 7 cases they used in addition the method described by Landis (*Amer. J. med. Sci.*, 1937, **193**, 297), which consists in applying a pressure of 40 mm. Hg for half an hour to the arm, and then drawing off blood from the area of venous stasis; by means of a haematocrit the amount of serum lost through transudation from a given volume of blood is estimated, plasma proteins are estimated by colorimetry, and from the haematocrit reading and plasma protein level the amount of protein which has escaped through the capillary walls into surrounding tissues can be calculated.

In normal subjects the test should cause little or no transudation of serum and no passage of plasma proteins through the capillary walls. In 6 of the 7 cases in which the method of Landis was used the test result was strongly positive, with considerable escape of proteins. The only negative result, however, occurred in a child who was severely ill, and who also showed normal or even increased capillary resistance in response to the negative-pressure test.

The authors therefore confirmed that, as a rule, capillary resistance is diminished in cases of rheumatic fever. They found, however, that the resistance may go on decreasing even though there is a good clinical response to treatment with amidopyrine, and that the degree of impairment of capillary resistance is not correlated with the severity of the disease. Its estimation is therefore of no prognostic value. They conclude that their experiments show that disturbance of capillary function is undoubtedly a factor in the pathogenesis of acute rheumatic fever, but that it does not, by itself, offer a satisfactory explanation of the tissue damage present in rheumatism. *Marianna Clark*

CHRONIC RHEUMATISM

1087. **Heberden's Nodes and Cervical Spondylarthrosis.** [In English]
P. PELTOLA and A. AHTO. *Annales medicinae internae Fenniae* [*Ann. Med. intern. Fenn.*] **42**, 64–74, 1953. 2 figs., 16 refs.

At the Kivelä Hospital, Helsinki, the authors investigated the relationship between Heberden's nodes and a localized condition of osteoarthritis which, in some cases, had been observed in the region of the 5th to the 7th cervical vertebrae and which, they suspected, might have irritated or compressed the main nerve trunks supplying the hand. Radiological examination of the cervical spine in 207 patients with well-developed Heberden's nodes revealed osteoarthritic changes in this region in more than 90% of patients in each age group over 40 years. In patients with nodes on the fingers of one hand only, the spondylarthrosis was con-

fined to that side of the spine, and encroachment on the intervertebral foramina was clearly demonstrated.

W. S. C. Copeman

1088. **Marie–Strümpell Spondylitis in Women**

T. L. Tyson, W. A. L. Thompson, and C. Ragan. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **12**, 40–42, March, 1953. 5 refs.

Marie–Strümpell arthritis seems to follow a more benign course in women than in men. Apart from the more frequent symptomatic involvement of the cervical region and *x*-ray evidence of involvement of the symphysis pubis, there seems to be little difference in the clinical picture in males and females. The somewhat less severe character of the disease in women may lead to errors in diagnosis or even to misdiagnosis; but this does not seem to be the cause of the relative infrequency with which the disease is reported in women. This series of cases shows that the disease does appear in women and should be included in the differential diagnosis of all complaints referable to the spine.—[Authors' summary.]

1089. **Radiotherapy in Arthritis**

M. H. L. Desmarais. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **12**, 25–28, March, 1953. 5 refs.

Previous reports have agreed about the beneficial effects of *x*-ray therapy in ankylosing spondylitis and in osteoarthritis, but regarding its benefit in rheumatoid arthritis they have been conflicting. The author therefore carried out a planned and controlled experiment at the Royal National Hospital for Rheumatic Diseases, Bath, in order to re-assess the value of *x*-ray therapy in these diseases. The 788 cases, which were selected at random, were treated mainly by high-voltage therapy using small, medium, or large doses, although some cases of spondylitis were given low-voltage therapy; technical details are given. In a control group the same routine was followed but the current was not switched on. All cases received physiotherapy.

The best results (assessed after 3 months) were obtained in ankylosing spondylitis (102 cases), relief of pain beginning about half-way through the course and reaching a maximum a few weeks after its completion. Large doses were only slightly superior to medium doses, low doses were less satisfactory, and with low-voltage therapy there was no response. In osteoarthritis (429 cases) the results with small and medium doses were not significantly different from those in the control series, but with large doses the relief of pain was sometimes dramatic, and a later follow-up showed that after 1 year 77% of these patients had maintained the improvement noted at 3 months.

In rheumatoid arthritis (257 cases) the results with all dosage schemes were disappointing, being not significantly better than those in the control group. In discussing this form of treatment in rheumatoid arthritis the author points out that joints may in fact flare up under *x*-ray therapy, and concludes that it should be used only when the disease is quiescent, and then in large doses. It is stressed that deep *x*-ray therapy, though useful, should be regarded only as an adjuvant to other forms of therapy.

Kenneth Stone

1090. **Clinical Studies of Phenylbutazone (Butazolidin) and Butapyrin (Irgapyrin) in Rheumatoid Arthritis, Rheumatoid Spondylitis, and Gout**

E. G. Kidd, K. C. Boyce, and R. H. Freyberg. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **12**, 20–24, March, 1953. 2 figs., 15 refs.

At the Hospital for Special Surgery (Cornell University Medical College), New York, the effect of phenylbutazone was studied in 51 patients with rheumatoid arthritis, in 13 with rheumatoid spondylitis, and in 16 with acute gout. Butapyrin—aminopyrin dissolved in phenylbutazone—was also tried in a smaller number of patients, but its use was discontinued because of its greater toxicity.

Phenylbutazone, 400 to 800 mg. daily in divided doses by mouth or 400 to 1,000 mg. intramuscularly once or twice daily, had a marked analgesic effect in 6 patients (11·6%), and a moderate effect in 16 patients (32%) with classical rheumatoid arthritis. Marked relief occurred much more often in acute gout and in spondylitis, being noted in 9 (58%) and 8 (61%) patients respectively. In acute gout the effect was rapid and dramatic, relief beginning within 24 hours. This improvement was accompanied by a decrease in the plasma uric acid level without significant increase in urinary uric acid. Reduction in plasma uric acid was also observed after the administration of phenylbutazone in cases of rheumatoid arthritis. It is suggested that this phenomenon may be a key to the further understanding of the fundamental metabolic defect in gout. Experiments, which are described, showed that the drug had no effect on plasma uric acid *in vitro*.

Toxic effects occurred in 26·7% of patients receiving phenylbutazone and in 68% of those given butapyrin. The most frequent symptoms were nausea, anorexia, vomiting, epigastric pain, and diarrhoea. Oedema and dermatitis occurred less frequently. Gastro-intestinal symptoms were not observed when the drug was given intramuscularly, but irritation at the site of injection made administration by this route impracticable.

Kenneth Stone

1091. **Effects of ACTH on the Peripheral Blood Flow in Rheumatoid Arthritis**

J. W. Beattie and A. Woodmansey. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **12**, 43–45, March, 1953. 3 figs., 10 refs.

The effect of the intravenous administration of corticotrophin (ACTH) on the skin temperature of 29 female patients with chronic rheumatism was studied at the Royal Bath Hospital, Harrogate, and University of Leeds. The majority of the patients had rheumatoid arthritis, but some had osteoarthritis [the number in each group is not stated]. The skin temperatures on the forehead, the flexor surfaces of both thumbs, and one great toe were recorded over a period of 30 minutes with the patient at rest in a room kept at 18·3° to 19·0° C. As a test of thermal response one foot was then immersed in water at 44° C. and the skin temperatures recorded as before for another 30 minutes. This procedure was repeated after intravenous infusion of 20 mg. of ACTH in 1 litre of a glucose–saline mixture; in some cases a

dose of 5 or 10 mg. was given. The infusion was started on the day before the skin temperatures were recorded and usually lasted 12 to 24 hours.

The thermal response in the foot in each case was assessed numerically, the " index " being the gradient of the temperature curve in degrees or fractions of a degree C. per minute. This was counted from 19° C. (the room temperature) to the peak of the rise (or if the peak was not attained, to the temperature rise at the end of 30 minutes of immersion) divided by the time in minutes. In 19 of the cases the average response was 0·23° C. per minute before administration of ACTH and 0·43° C. afterwards. In 12 of these 19 cases the toe temperature was higher (average 2·9° C.) during the resting period after administration of ACTH than it was before. In a further 5 of the 29 cases there was no change in the thermal response after ACTH but there was a higher resting skin temperature in some digits of the upper or lower limbs. In the remaining 5 cases in the series the ACTH had no effect.

The skin temperature changes brought about by intravenous administration of ACTH indicated that the peripheral blood flow was modified in two ways: first, peripheral vascular tone was reduced and cutaneous blood flow increased; secondly, and more important, a previously sluggish thermal response was improved. As the accelerated thermal response in the other limbs was the result of a stimulus in one, the authors suggest that the effect is neurovascular " via the thermo-regulatory mechanism ". *K. C. Robinson*

1092. **Placental Blood Serum in the Treatment of Rheumatoid Arthritis. Preliminary Report**
M. SPIELBERG. *Archives of Internal Medicine* [*Arch. intern. Med.*] **91**, 315–324, March, 1953. 10 refs.

A therapeutic trial of placental blood serum in the treatment of rheumatoid arthritis, based on the well-known beneficial effect of pregnancy, is here recorded. The placental blood was collected aseptically immediately after a birth, the amount obtained varying from 20 to 100 ml. Exact details are given of the preparation of a pooled and filtered serum, tested for sterility and serologically for syphilis. No placental blood was taken from a mother who was Rh-negative, or who had a history of syphilis or a positive Wassermann reaction.

At the Arthritis Clinic, Jewish Hospital of Brooklyn, New York, 15 female patients with rheumatoid arthritis were the subjects of an adequately controlled study. Definite improvement was noted in 10 patients, beginning as early as the second day in 3 cases, and in 9 within the first week. The optimum effect of the treatment was obtained by giving 30 ml. of the placental serum intravenously daily for the first 2 weeks, 30 ml. 3 times a week for the next 2 weeks, then twice a week for 3 more weeks, and finally 30 ml. once a week for 1 to 3 weeks. The improvement observed included reduction of joint stiffness, of tenderness and swelling, of pain on movement, and of muscle spasm, improvement in muscle tone and mobility, increased sense of well-being, more restful sleep, improved appetite, and improved ability to carry out everyday duties. The microcytic hypochromic anaemia responded without other treatment, and the erythrocyte sedimentation rate fell to normal in 2 cases.

The 5 patients who showed no response were all in the post-menopausal age group, and the duration of their disease varied from 6 to 31 years. Of the 10 patients who improved, 3 had complete remission, 3 major improvement, and 4 minor improvement. One patient who had derived no benefit from cortisone, and 2 who had suffered toxic side-effects with cortisone, responded very well to placental blood serum. Administration of the serum can be stopped without relapse. So far, improvement has been maintained for 6 months, but further observation is needed to determine its maximum duration; no toxic side-effects have been noted. It is considered that these results suggest that the active therapeutic principle is not cortisone or corticotrophin. Four illustrative case histories are recorded.

Kenneth Stone

1093. **Proseptasine in the Treatment of Rheumatoid Arthritis**
L. J. BARFORD. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **12**, 35–37, March, 1953. 5 refs.

The author has treated 59 patients with rheumatoid arthritis, most of whom were out-patients at the East Surrey Hospital, Redhill, Surrey, with a prolonged course of benzylsulphanilamide (" proseptasine ") in doses ranging from 0·5 g. three times daily to 0·25 g. twice daily, combined with a vitamin-B supplement. The duration of treatment varied from one to 46 months, in 12 cases continuing for one year or longer. The results were classified as " improved ", " unchanged ", or " worse " on the basis of the following criteria: nature and degree of disability, degree of joint pain, appearance of the joint, joint tenderness, and range of movement. [Details of the method of this assessment are not given.]

Treatment was abandoned in 5 cases owing to the development of minor toxic effects, and 10 further cases were excluded from the analysis as their follow-up was incomplete. Of the remaining 44 cases, 32 improved, 11 remained the same, and one deteriorated; of the 12 cases under treatment for one year or more, 11 improved. There was a high relapse rate when the drug was withdrawn, but a similar response when it was reinstated. There was no constant effect on the erythrocyte sedimentation rate, and blood counts showed no gross abnormality after prolonged continuous treatment. The improvement rate in this series was 65%, which corresponds closely with other reported results of prolonged continuous sulphonamide therapy. *K. C. Robinson*

1094. **Effect of an Anti-histamine in Rheumatoid Arthritis**
D. C. WILSON. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **12**, 38–39, March, 1953. 1 ref.

An investigation into the usefulness of " phenergan " in the treatment of rheumatoid arthritis is described. Eleven cases (ten rheumatoid) were treated. There was a uniform lack of objective response. The results are compared with those obtained in infective arthritis.—[Author's summary.]

1095. **Gold, Sodium, and Liver Function in Rheumatoid Arthritis**
G. D. KERSLEY, L. MANDEL, and M. R. JEFFREY. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **12**, 29–31, March, 1953. 5 refs.

In 1946 Selye (*J. clin. Endocr.*, **6**, 117) reported that diets rich in sodium tended to precipitate the diseases of adaptation, while acidifying salts, such as ammonium chloride, tended to inhibit them. An investigation was carried out at the Royal National Hospital for Rheumatic Diseases, Bath, designed to show whether a low-salt diet and the administration of acidifying drugs would increase the beneficial effects of gold treatment in rheumatoid arthritis. Three groups of patients received a 5-month course of gold therapy while kept on a low-salt diet; in addition the three groups were given, respectively, sodium chloride, ammonium chloride, and an inert control substance (lactose). The results were the same in each group, about 50% of the patients being much improved. There was no evidence of any enhanced effect from either the sodium or the ammonium chloride, nor was there any evidence of impaired liver function, as determined by liver function tests. *H. F. Turney*

1096. **Rheumatoid Arthritis and the Liver.** [In English] O. LÖVGREN. *Annales medicinae internae Fenniae* [*Ann. Med. intern. Fenn.*] **42**, 42–51, 1953. 14 refs.

In view of the fact that when acute hepatitis supervenes in rheumatoid arthritis there is often relief of joint pain, a special study has been made at St. Erik's Hospital, Stockholm, of the connexion between disordered hepatic function and rheumatoid arthritis. The author had previously drawn attention to the low serum iron and citric acid levels in rheumatoid arthritis, and he later found that in acute hepatitis the exact opposite prevailed. This led him to suspect some physiological antagonism between the two disease conditions, the cause of which might be found in the liver.

The hippuric acid test was carried out on 30 patients with rheumatoid arthritis, and in 10 evidence of gross liver damage was found. The results of the phosphatase test were negative in all the patients, while the thymol reaction was positive in over half of them. Of 93 cases of rheumatoid arthritis seen post mortem, liver damage was found in 52, while of 13 patients on whom liver biopsy was performed, definite histological changes of a pathological nature were found in 7.

W. S. C. Copeman

1097. **Chronic Rheumatic (Rheumatoid) Diarthritis and the Shoulder–Hand Syndrome**
M. KELLY. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 330–334, March 7, 1953. 3 figs., 14 refs.

In a previous paper (*Med. J. Aust.*, 1952, **2**, 79) the author attempted to show that chronic rheumatic or rheumatoid monarthritis could not be clearly differentiated from rheumatoid polyarthritis. In the present paper he first points out that rheumatoid arthritis may persist for years in two joints without spreading to others, but that in rheumatoid diarthritis two unrelated joints are involved at the same time and, most commonly, either the neighbouring joint or the corresponding joint on the opposite side of the body is affected. The exception to this generalization is to be found in the shoulder–hand syndrome, the elbow being unaffected in this condition.

The author briefly describes 15 cases of diarthritis to demonstrate that the arthritis may remain confined to the two joints, may subside, or may later spread to many joints. In his view the shoulder–hand syndrome, which was present in 2 of these cases, may be merely a stage during the onset of rheumatoid polyarthritis or a stage during remission. The swelling of the hand and stiffness of the fingers in this condition are usually secondary to arthritis of the wrist or of the metacarpo-phalangeal joints.

Infective arthritis (involving a few large joints) and true rheumatoid arthritis (with onset in the hands and toes and marked symmetry) cannot, in the author's view, be distinguished as separate entities. *C. E. Quin*

1098. **Cardiac Lesions in Rheumatoid Arthritis** (Lesiones cardíacas en la artritis reumatoidea)
M. JOSELEVICH and L. SUCARI. *Prensa médica argentina* [*Pren. méd. argent.*] **40**, 679–689, March 20, 1953. Bibliography.

The authors begin by questioning the possibility of any aetiological relationship between rheumatic fever and rheumatoid arthritis, especially in view of reports in the recent literature on the cardiac complications of the latter condition. According to them, most European authorities believe they have a common aetiology, whereas most workers in North America (exceptions are mentioned by name) hold the opposite view. The pros and cons of each theory are discussed. One possibility is that the disease attacks the brain and heart in the younger age group, whereas in older subjects the joints bear the brunt. The incidence of cardiac lesions in rheumatoid arthritis as reported in the literature has varied from 2% to 63%. In one controlled series, in which patients who were over 50 years of age or who had any "non-rheumatic" type of heart disease were ruled out, it was found that 35·8% of the remaining cases had some cardiac anomaly. It is obvious from these figures that very little agreement has been reached on this question.

The authors then describe 6 cases of rheumatoid arthritis and 2 of non-rheumatoid arthropathies, associated in all cases with heart disease, including one case of chronic cor pulmonale, another of calcified pericardium, and 2 of "chronic aortitis". In one case of gout there was an apical systolic murmur. From these cases it is concluded that rheumatoid arthritis may be complicated by cardiac disease of varied aetiology, and from this variation arises the difficulty of arriving at any definite conclusion.

[This must surely result when authors choose to base their conclusions on a total of 8 patients of whom 5 were well over the age of 50; it must be obvious that the problem of this relationship cannot be solved by including degenerative cardiac lesions, and that far larger series and younger patients must be studied]

Paul B. Woolley

Traumatic Surgery and Orthopaedics

1099. **Fat Embolism**
W. W. GLAS, T. D. GREKIN, and M. M. MUSSELMAN. *American Journal of Surgery* [*Amer. J. Surg.*] **85**, 363–369, March, 1953. 31 refs.

In their prefatory remarks to this paper, in which they describe a study to determine " how common fat embolism is and how sick it makes people ", the authors pose the question, " How can the opinion of Warren (*Amer. J. Path.*, 1946, **22**, 69), who believes that fat embolism is an important cause of death, be reconciled with that of Whitson (*J. Bone Jt Surg.*, 1951, **33A**, 447), who believes that the diagnosis of fat embolism as a cause of sudden death should be discontinued?"

In an attempt to clarify the position 109 patients consecutively admitted to Wayne County General Hospital, Eloise, Michigan, with moderate or severe injuries were studied. Urine was collected over the 24 hours for the first 15 days and examined for free fat. Patients were examined for pulmonary and cerebral symptoms, and radiographs were taken of the chest in all patients whose urine contained fat. Of all patients 52% were found to have fat in the urine, the figure being 55% for the more severely injured patients. Fat was also found in 57% of patients with burns and in 25% of those with lacerations. Fat embolism was considered a major factor in causing death in 57 cases. The sputum of 50 patients with non-traumatic illness was examined for fat and the findings compared with those in the urine. Fat was found in the sputum in 32% of these cases, but in the urine in only 2%.

In discussing the mechanism of formation of fat emboli the authors point out that most workers hold the view that fat globules gain access to the circulation by way of disrupted veins, whereas others consider that a disturbance of plasma fat emulsion is implicated. With this in mind they carried out experiments on rabbits to determine the effect of stress on the emulsion of fat in the blood stream, but failed to find any alteration in the turbidity of the serum or in the level of lipids in the blood.

A review of their own findings in the light of those reported in the literature leads the authors to the following conclusions. Fat embolism is of importance and relative frequency, but its occurrence is not related to the extent of the injury sustained. Many patients with rather mild symptoms recover and the nature of their condition goes unrecognized. Determination of fat in the urine is a satisfactory test, positive results often being obtainable on the first day after injury. Fat is so frequently found in the sputum in other conditions that its presence is an unreliable indication in the diagnosis of fat embolism. There is no evidence that chylomicrons in the blood coalesce to form masses or that shock has any effect in this connexion. Fat embolism is not found postoperatively where the medullary fat has not been interfered with; where fat embolism is present the fat probably gains direct access to the blood stream. The discrepancy between the amount of fat released by trauma and that necessary to cause symptoms has been explained in several ways: although it was formerly believed that hydrolysis occurred, it has since been shown that the fat globules present consist of neutral fats.

As regards the treatment of these cases, it is suggested that theoretically an emulsifier should help, but that one suitable to be added to the blood stream has not yet been found. *J. G. Bonnin*

1100. **Secondary Tenorrhaphies and Tendon Grafts in Injuries to the Hand**
J. L. POSCH. *American Journal of Surgery* [*Amer. J. Surg.*] **85**, 306–318, March, 1953. 12 figs., 13 refs.

Tendons of the hand may be injured in several ways, the most common being by direct trauma with severance of the skin and underlying tendons. In this paper from Detroit, Michigan, 23 cases of such injury are presented and the methods of repair described.

The author considers that early diagnosis is essential, commenting that physiological testing is sufficient to identify the lesion. He regards loss of flexion of the terminal phalanx as indicating division of the flexor profundus; loss of flexion of the entire finger as indicating division of the flexores profundus and sublimis; and loss of flexion of the metacarpo-phalangeal joint and inability to extend the interphalangeal joints as indicating injury to the lumbricals or interossei. A tendon that has been partially severed may rupture when activity is resumed, and to avoid this possibility he advises that flexion should be tested against pressure, partial division being indicated by failure of the patient to exert force. He recommends that primary repair should not be carried out if the wound is several hours old or has been interfered with in any way, nor if there is an associated fracture; secondary repair may be carried out in 3 to 4 weeks if the skin is well healed and there is no redness or induration. He considers that grafts do better in these cases than secondary tendon suture, and that to be suitable for reconstructive surgery a patient must be keen and co-operative and have good skin, good joints, and good sensation. The younger the patient, he says, the better the result. He considers that sensation is most important, and that digital nerves should be repaired at the time of primary wound closure. In severe injuries amputation should be considered. Despite unfavourable reports of tendon grafting in the little finger, the author has successfully performed this operation in a number of cases, and although some difficulty in flexing the terminal phalanx has resulted, the strength of the finger has been improved. Occasionally he has advanced the flexor profundus to the distal phalanx with good results.

Operative Technique.—In reconstructive surgery the author regards a bloodless field and the use of small

instruments as essentials. He recommends that incisions in the hand should follow the flexion creases, except in operations for the removal of the palmaris longus, when a longitudinal incision is made along the length of the tendon. For grafts he prefers the extensor tendons of the toes, as these are smaller and have some para-tendon. Tendon " pulleys ", if destroyed, can be reconstructed with tendon or by sewing the flexor sublimis attachments together to form a bridge. He considers that determination of the tendon length is important, and states that toe extensor-tendon grafts tend to contract more than sublimis grafts. In applying tendon grafts obtained from the foot he employs Bunnell's method, in which, with finger and wrist straight, the tendon is sutured in slight tension. No. 6 eye silk is used for peripheral nerves. The skin is closed with cotton sutures, and small rubber drains are inserted; these are removed after 24 hours. The wrist and fingers are placed in moderate flexion, a little early movement being encouraged but not insisted on. At the end of 3 weeks the hand is exercised in warm soapy water once a day. Return to work is usual within 6 to 8 weeks. *J. G. Bonnin*

1101. **Fracture of the Neck of the Humerus with Dislocation of the Head Fragment**
C. S. Neer, T. H. Brown, and H. L. McLaughlin. *American Journal of Surgery* [*Amer. J. Surg.*] **85**, 252–258, March, 1953. 10 figs., 14 refs.

The head of the humerus when shattered falls into 4 fragments related to the epiphysial lines—namely, the anatomical head, the greater tuberosity, the lesser tuberosity, and the shaft. Unfortunately, descriptions of fracture-dislocation are not uniform and results are difficult to compare. It has been claimed that fracture of the neck with dislocation forms 1·1% of fracture-dislocations of the upper end of the humerus. According to the present authors, fragmented fractures fall into two groups: Group I consists of those in which the head remains inside the capsule, and Group II of those where the head is outside the capsule. In either group the fracture may be impacted or unimpacted.

In this paper 20 cases of Group-II fractures seen at the Presbyterian–New York Orthopedic Hospitals, New York—of which 17 were of anterior and 3 of posterior dislocation—are discussed. (In posterior dislocations the head is damaged by contact with the posterior margin of the glenoid.) The following lines of treatment were adopted, a second operation being necessary in those cases in which the first one had proved unsuccessful: closed reduction, 6; open reduction, 3; removal of the head, 16 (with reconstruction in 8); fusion 1. Closed reduction was successful in only 2 cases, the head fragment slipping out of position and having to be removed in 4. Open reduction resulted in failure in all 3 cases in which it was performed. After 5 of 19 resections some bony bridging developed between the humerus and scapula, but function was poor. Repair of the musculotendinous cuff did not improve the result. The authors found that primary arthrodesis was difficult to accomplish and that vascular necrosis may occur after any procedure. They recommend that impacted fractures should be reduced by open or closed methods, and that unimpacted fractures are best treated by simple excision.

[Replacement of the humeral head with a prosthesis is amply justified by this tale of disappointment; and while it is true that its place in the treatment of complex fracture-dislocations has not yet been fully evaluated, the known results are better than those described in this paper.] *J. G. Bonnin*

1102. **Treatment of Burns and their Complications**
J. T. Rush. *American Journal of Surgery* [*Amer. J. Surg.*] **85**, 187–193, Feb., 1953. 9 figs., 9 refs.

The author describes the treatment of burns by exposure to the open air, without dressings, in 186 cases. It is concluded that with this method there is less discomfort, infection, and scarring, more rapid healing or earlier delineation of full-thickness loss of skin, and less anaemia and malnutrition. He emphasizes that movement in affected joints must be established and maintained, and that there is no contraindication to putting the patient in a bath to remove necrotic tissue. *Dennis Walker*

1103. **Streptokinase–Streptodornase in the Local Treatment of Burns**
F. E. Stein, L. T. Wright, and A. Prigot. *Harlem Hospital Bulletin* [*Harlem Hosp. Bull.*] **5**, 134–146, March, 1953. 17 figs., 11 refs.

In this article are recorded clinical observations on the local application of streptokinase–streptodornase (SK–SD) in a jelly base to 6 children suffering from burns of all degrees treated at Harlem Hospital, New York, in 1952. Intravenous administration of fluids, blood transfusion, and antibiotic therapy were also used when indicated.

The origins and modes of action of SK–SD are explained. It is claimed that the enzymes speed up the separation of sloughs, and that the breakdown products may play a part locally in the regeneration of tissue. Details of the preparation and reconstitution of the products used in this study are given. The material was applied direct to the burn area, and covered with sterile gauze, sheet wadding, and stockinet as needed. The dressings are described as " adhesive to coaptation ", but no sealing with cement was used. Burns were redressed every 2 or 3 days and debridement by sharp dissection was performed as necessary. None of the burns was treated with SK–SD *ab initio*.

The authors, who have used other methods from time to time, consider that there was less smell, irritation, and toxaemia in these cases, and the patients were out of bed earlier. Second-degree burns were healed in 8 to 16 days, and in third-degree burns sloughs could be separated in 7 to 10 days and healthy granulation tissue ready for grafting appeared within 14 days. There was only one fatality, in a girl of 6 with severe burns involving 60 to 70% of the body surface who died from toxaemia 84 days after burning.

[It is hoped that the authors will publish results in a larger series of cases treated with SK–SD, together with a control series treated by another method.]
John Huston

Neurology and Neurosurgery

1104. **Blood Plasma in Multiple Sclerosis. Periodic Abnormalities in Pattern of Paper Chromatograms**
R. L. SWANK. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **69**, 281–292, March, 1953. 7 figs., 13 refs.

In this work, carried out at McGill University and the Montreal Neurological Institute, the plasma protein patterns in 21 normal subjects and in 41 cases of disseminated sclerosis were compared. Two-dimensional ascending paper chromatograms of the plasma proteins were obtained at weekly intervals for periods varying from 3 weeks to 5 months.

Of the 243 chromatograms from the normal subjects, 81% showed a regularity of pattern (classed as normal) and contained 15 to 20 or more components, the height of most of which was greater than the width. In 4% there was an abnormal pattern, the number of fractions being decreased and many of them being short and broad. The remaining 15% showed borderline patterns. Abnormal or borderline patterns occurred in normal persons suffering from the common cold and also, in many of the women, at the onset of menstruation. In fact, most of the normal subjects showed borderline abnormality at some time during the period of study, the abnormalities tending to recur periodically at about monthly intervals. In 3 of them who showed many abnormal patterns, one was an apparently healthy male, but the other 2 were found to be sisters of a patient with disseminated sclerosis.

In the patients a total of 437 chromatograms were obtained, 34% of which were normal, 32% borderline, and 34% abnormal. Most of the patients showed both normal and abnormal records, the abnormal ones appearing in cycles of 1 to 3 months and lasting 1 to 4 weeks. In one patient, studied during pregnancy, 15 out of 19 chromatograms were abnormal. There was, however, no correlation between the occurrence of abnormal chromatograms and the clinical activity of the disease, nor with the erythrocyte sedimentation rate.

M. Lubran

1105. **Idiomuscular Contraction and its Clinical Significance.** (De idiomusculaire contractie en haar waarde voor de cliniek)
A. K. J. KOUMANS. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **97**, 727–733, March 21, 1953. 22 refs.

Hypotheses on the causation of idiomuscular contraction are reviewed and personal observations on malnutrition in Asian migrants entering Sumatra are recorded. From these, and from findings reported in the literature on malnutrition in prison camps and during the period of food shortage in western Holland at the end of the last war, the author concludes that idiomuscular contraction is not exclusively a feature of neurological disorder, but that it may result from local changes in the muscle tissue itself as a consequence of protein deficiency.

Apart from gross deficiency, it is emphasised that hypoproteinosis is an extremely widespread condition, and its clinical manifestations many and varied. Since testing for idiomuscular contraction is extremely simple, its recognition may well prove of value in detecting hypoproteinosis in its early stages, before oedema and measurable biochemical changes have become manifest.

Adrian V. Adams

1106. **Is Idiomuscular Contraction a Physiological Phenomenon?** (Is de idiomusculaire contractie een physiologisch verschijnsel?)
G. P. M. HORSTEN and R. LUIJKEN. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **97**, 733–735, March 21, 1953. 1 fig., 7 refs.

In the authors' opinion, the old view that idiomuscular contraction indicates a disease state, such as tuberculosis, cachexia due to other causes, or a specific nutritional deficiency, must be rejected. Although more often to be elicited in undernourished subjects, they found that it could be evoked in 55% of the apparently normal personnel of two physiological laboratories at the University of Amsterdam.

By means of an electromagnetic device (which is fully described) taps of constant magnitude were delivered from a patella hammer to the skin of the upper arm of 58 subjects. Marked idiomuscular contraction was evoked in 9 of these, moderate contraction in 23, and no contraction in 26. From measurements of skin creases of subjects in each of these three groups an index was obtained of the mean thickness of the subcutaneous fat in the region stimulated. The statistical correlation between this index and idiomuscular contraction was found to be highly significant. *Adrian V. Adams*

1107. **The Use of Protective Inhibition in the Treatment of Organic Lesions of the Nervous System.** (Применение метода охранительного торможения в клинике органических поражений нервной системы)
N. A. KRYSHOVA. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **53**, 24–28, Jan., 1953. 1 ref.

The author reports the satisfactory results obtained with sleep therapy in the treatment of narcolepsy and catalepsy. The methods employed included appropriate adjustments and ward arrangements, enforcement of silence, darkening of the rooms, sound-proofing, the employment of monotonous repetitive stimuli, and the use of the smallest effective doses of hypnotic drugs. Conditioned-reflex techniques were likewise used as partial substitute for these drugs. Encouraging results were also obtained in the treatment of phantom and

thalamic pain. Prolonged remissions of the disease followed its use in disseminated sclerosis. The favourable effect of " dimedrol " [the Russian name for diphenhydramine] in infective conditions of the nervous system may also, it is thought, be due in part to its hypnotic effect. The intravenous injection of bismuth carbonate probably leads to protective inhibition in the cerebral cortex by the mechanism of induction. It has therefore been tried by the author in cases of post-encephalitic Parkinsonism. In a series of 130 cases some improvement was obtained in 81%. *L. Crome*

1108. **The Employment of Sleep Therapy in Organic Nervous Diseases.** (К вопросу о применении терапии сном в клинике органических нервных болезней. Следовые реакции в зрительном анализаторе и некоторые другие данные корковой динамики у больных с органическими заболеваниями нервной системы в связи с терапией сном.)
Y. M. KRAYEVSKI. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **53**, 29–36, Jan., 1953. 8 figs., 17 refs.

Sleep therapy was employed in a series of 120 patients with various neurological disorders. It was found useful in migraine, cerebellar disorders, disseminated sclerosis, narcolepsy, and some spinal diseases. It is contra-indicated in severe hypertension with involvement of the somatic viscera, in pulmonary and renal disease, and in heart failure. It is stressed that it is important to select the appropriate hypnotic drug and adjust its dose carefully and individually for each patient. Reduction of the dose is often more useful than its increase in refractory cases.

The treatment described was accompanied by a physiological investigation of patients, a study being made of contrast phenomena with the visual analyser in which the perception of alternate black and white squares was observed. It was found that these reactions became more normal in a number of successfully treated patients. *L. Crome*

1109. **Anomic Aphasia. Differential Diagnosis and Cerebral Localization of Lesion in Twenty Cases**
C. SUTER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 462–468, Feb. 7, 1953. 4 figs., 10 refs.

The author, working at the University of Virginia Hospital, Charlottesville, suggests the term "anomic aphasia " for the speech disorder characterized by difficulty in recalling names of persons and things. [The condition is usually known in Britain by Head's term " nominal aphasia ".] The three major types of aphasia are classified as: (1) motor aphasia, caused by a lesion of Broca's area; (2) sensory aphasia, which includes the various forms of inability to understand the spoken or written word, the severest being " jargon " aphasia; and (3) anomic aphasia.

The author believes that anomic aphasia is due to a lesion of the dominant hemisphere in the region of the supramarginal gyrus, the angular gyrus, and the posterior part of the first, second, and third temporal gyri (Brodmann's areas 40, 39, 37 and posterior parts of 21 and 22). He emphasizes the frequency with which homonymous hemianopia is associated with anomic aphasia. In an analysis of 20 cases he found 14 in which there was some defect in the visual fields. The anomic aphasia was due to vascular lesions in 10 of the 20 cases and to tumours in the other 10. The condition was diagnosed as motor aphasia in half the cases, and the author suggests that the differential diagnosis of anomic aphasia is insufficiently understood.

[This paper confirms Head's classical work on aphasia, and there seems to be no valid reason for substituting " anomic " aphasia for Head's term " nominal " aphasia.] *N. S. Alcock*

1110. **The Treatment of Parkinsonism with a New Antispasmodic Compound: a Preliminary Report**
K. R. MAGEE and R. N. DEJONG. *University of Michigan Medical Bulletin* [*Univ. Mich. med. Bull.*] **19**, 59–61, March, 1953. 1 fig.

A new antispasmodic, " Compound 08958 ", with the chemical formula 1-phenyl-1-*cyclo*pentyl-3-piperidino-1-propanol hydrochloride, and therefore related to " artane ", was tried in 48 cases of Parkinsonism at the University Hospital, University of Michigan.

In just over half of the cases of idiopathic and post-encephalitic Parkinsonism the results, objective as well as subjective, were better than those obtained with artane or hyoscine; in a further one-quarter the results were as good. The compound was considerably less effective than other drugs in arteriosclerotic Parkinsonism. The chief effect of the compound was the relief of rigidity, but many patients felt that the tremor was materially improved. In 4 cases there was a remarkable decrease in the frequency of oculogyric crises. There was no improvement in one case each of familial tremor, senile tremor, congenital athetosis, and spastic pseudosclerosis.

The recommended dose of Compound 08958 is 2·5 mg. once a day, increasing by 2·5 mg. every second or third day to the limit of tolerance. Side-effects were more evident than after administration of artane, though the postencephalitic group of patients tolerated the drug better than the others. Side-effects included dryness of the mouth (14 cases), dizziness (13 cases), and blurred vision (5 cases). Nausea, weakness, and epigastric discomfort occurred in a few cases, but the only serious complication was acute delirium after large initial doses. *L. G. Kiloh*

CEREBROVASCULAR DISORDERS

1111. **The Syndrome of Traumatic Intracerebellar Hematoma, with Contrecoup Supratentorial Complications**
R. C. SCHNEIDER, L. J. LEMMEN, and B. K. BAGCHI. *Journal of Neurosurgery* [*J. Neurosurg.*] **10**, 122–137, March, 1953. 12 figs., 26 refs.

The authors report in detail 4 cases of head injury complicated by cerebellar and supratentorial haematoma. All cases were operated on at the University Hospital, Ann Arbor, Michigan, and intracerebellar blood clots

removed. Explorations were also made in other sites, both frontal and temporal, and various combinations of subdural recovery and intracerebral clots were found; 3 of the patients made a good recovery.

The diagnosis and treatment of this complication is discussed. It is stressed that in many cases there are no definite localizing signs pointing to the posterior fossa as the site of a haematoma. But the diagnosis should always be considered when the level of consciousness is deteriorating after injury and there are no signs suggestive of a supratentorial lesion. Scalp contusions and fracture lines in the posterior fossa are helpful indications of the site of the lesion. Whether or not a haematoma is found in the posterior fossa in such cases, it is recommended that there be no delay in making further exploration in the temporal and frontal regions if the patient's condition does not improve. *Brodie Hughes*

1112. **A Clinical and Experimental Determination of Pressure within the Carotid Arteries**

W. J. GERMAN and S. P. W. BLACK. *Yale Journal of Biology and Medicine* [*Yale J. Biol. Med.*] **25**, 245–249, Feb., 1953. 6 figs., 6 refs.

The empirical treatment of internal carotid aneurysm by proximal ligation has been evaluated at the Yale University School of Medicine by studying intra-arterial pressures. These were measured by means of an inductance-type gauge with amplifier recording on a photographic galvanometer, connexion with the manometer being made with an 18- or 19-gauge needle placed in the exposed carotid artery. A typical recording from one common carotid artery is shown, the pressure being 124/54 mm. Hg. When the artery was occluded proximally the pressure fell to 43/30 mm. Hg, and when the external carotid was also occluded the pressure was 31/29 mm. Hg. Emphasis is laid on the much greater reduction of the pulse pressure than of the mean or systolic pressure. The reduction in pressure persists for a significant length of time, as is illustrated in a case where the pressure was 72/56 mm. Hg one year after ligation of the common carotid artery; during this time there had been a great reduction of the patient's intracranial carotid aneurysm. Where total occlusion of the carotid artery was thought inadvisable, a partial ligation by several infolding mattress sutures was performed. This caused an immediate fall in pressure distally from 153/92 to 87/72 mm. Hg. In the only instance reported where the pressure was recorded 26 days after such a partial closure of the vessel the pressure was 120/88 mm. Hg, and complete occlusion then reduced it to 64/58 mm. Hg. [This would suggest that the reduction of pressure by partial occlusion is only temporary.] Similar recording of the changes of pressure due to occlusion of the carotid arteries was also made in dogs.

A brief discussion of these changes in pressure in relation to the stresses on aneurysmal sacs is included. These stresses are total hydrostatic pressure, pulsatile flow, jet action, and turbulence. It has been shown how hydrostatic pressure is reduced, and the pulsatile changes in flow are presumably also reduced proportionately with the pulse pressure. Jet action varies with the cube of the flow velocity, and so will also be greatly reduced distal to a ligation. [Changes in the factor of turbulence are not assessed.] Theoretical considerations, therefore, support the observed finding that carotid ligation reduces the stress on an aneurysm of the internal carotid artery of the same side. *Donald McDonald*

1113. **The Complications of Carotid Artery Ligation in the Neck**

C. E. BRACKETT. *Journal of Neurosurgery* [*J. Neurosurg.*] **10**, 91–106, March, 1953. 5 figs., 22 refs.

The author analyses the incidence and types of complication following ligation of the carotid arteries in the neck for intracranial vascular abnormalities, as observed in 65 patients undergoing this procedure at the Presbyterian Hospital, New York, in the period 1943–50. Cerebral complications developed in 21 cases (32%) and 6 patients died, a mortality of 9%. The complications all occurred in patients who had shown a negative Matas test after periods of compression varying from 10 to 30 minutes, although it has been claimed that a negative test result precludes the likelihood of complications. In a few patients carotid arterial pressures were also investigated before and after ligation, and it was established that a fall of carotid pressure after ligation was not a reliable indication of complications to come. The form of anaesthesia and the type of ligature used did not seem to have any particular significance, nor was the occurrence of complications related to the age of the patient.

The incidence of complications was high (3 cases) in a group of 5 patients undergoing ligation soon after a proven subarachnoid haemorrhage, while among 14 cases treated 14 days or more from the time of bleeding the incidence was low (6 cases). It was not clear, however, whether this was related to the time factor or to the type of case. It is concluded, however, that ligation during the time of active bleeding is a definite hazard. The incidence of complications was most closely related to the type and situation of the lesion. Cases with supraclinoid aneurysms or aneurysm on the communicating arteries showed the highest incidence after ligation, while infraclinoid aneurysms and lesions with an arteriovenous shunt seldom resulted in complications. Again, the incidence of complications was lowest after ligation of the internal carotid artery, but the author notes that this type of ligation was most often performed for infraclinoid aneurysms in which, as stated above, the incidence of complications was low in any case. He concludes that the particular artery ligated was not a significant factor in determining incidence.

The clinical features of the development of complications included headaches, mental confusion, motor and sensory hemiparesis, aphasia, and blindness. The onset, which took place within 12 hours of ligation in 17 cases, and after 18 hours in 4 cases, was usually sudden. A rise of arterial pressure was found in 9 of the 14 cases with complications (43%), as against 9% of the uncomplicated cases, and was considered to be a useful sign of impending complication. The aetiology of the complications is discussed. Persisting haemorrhage after

ligation did not appear to be present, nor could a diagnosis of thrombosis or embolism be established; in all cases in which the clip or ligature was removed the artery was found to be patent. There is strong presumptive evidence that ligation tends to produce vasodilatation rather than vasoconstriction. A theory is put forward that the reduced blood flow after ligation with an inadequate collateral circulation results in cerebral anoxia, oedema, and raised intracranial pressure. This process can be reversed by removal of the ligature, thus restoring the blood flow and cerebral oxygenation.

Cases for treatment by carotid ligation should be carefully selected, and those with cerebrovascular lesions in unfavourable positions or with inadequate collateral circulation should be excluded. After ligation, patients must be under constant supervision, their strength and responsiveness should be tested every 5 minutes for at least 12 hours, and instruments kept in readiness for immediate removal of the ligature. On the appearance of complications this should be done within 15 minutes if the result is to be effective. *Brodie Hughes*

CEREBRAL INFECTIONS

1114. **Treatment of Bacterial Meningitis of Unusual Etiology and Purulent Meningitis of Unknown Origin**
M. H. LEPPER, N. H. BLATT, P. F. WEHRLE, and H. W. SPIES. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **85**, 295–302, March, 1953. 4 refs.

The effect of various antibiotics in meningitis and a scheme of treatment appropriate to the infecting organism are described in this paper from the Municipal Contagious Disease Hospital, Chicago (University of Illinois). Patients were treated over a 2-year period, those suffering from pneumococcal, meningococcal, or influenzal meningitis being excluded from this study, as were those who had received treatment before admission to hospital.

In 21 of 41 patients the organism was identified by direct examination of the cerebrospinal fluid (C.S.F.); in the others no organisms were found on examination or culture of the C.S.F. In the former group the causative organisms were a haemolytic streptococcus (8 cases), coagulase-positive *Staphylococcus aureus* (3 cases), *Bacterium coli* (3 cases), *Klebsiella pneumoniae* (2 cases), and *Alcaligenes*, *Corynebacterium*, *Pseudomonas*, *Listeria*, and a mixture of *Pneumococcus* and *Bact. coli* (1 case each).

Soluble penicillin in a dose of 1 mega unit by intramuscular or intravenous injection every 2 hours for several days was effective against most of the Gram-positive cocci, but some staphylococci were resistant to penicillin, and other drugs had to be given. Chloramphenicol or aureomycin given intravenously 6-hourly to a total of 50 mg. per kg. a day was effective in influenzal meningitis and meningitis due to *Bact. coli*. The best results in meningitis due to *Klebsiella pneumoniae* were obtained with chloramphenicol.

Treatment in the second group of 20 cases depended upon the age of the patient and the severity of the disease. In children under the age of 10 years, chloramphenicol and aureomycin are recommended, with the addition of penicillin if the child is critically ill. In children over the age of 10 years penicillin is the drug of choice, with the addition of streptomycin if the child is severely ill. [The authors do not assess the value of sulphonamides either alone or combined with antibiotics. It should also be pointed out that because of the rapidly changing sensitivity of organisms to antibiotics the authors' conclusions may not be generally applicable.] *R. M. Todd*

1115. **Brain Abscess. Influence of the Antibiotics on Therapy and Mortality**
H. T. BALLANTINE and J. C. WHITE. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 14–19, Jan. 1, 1953. 4 figs., 3 refs.

The authors review two series of cases of brain abscess admitted to the Massachusetts General Hospital, Boston, in the 5-year periods 1936–40 and 1946–50 respectively. In the first series there were 31 patients with 25 deaths (80%), and in the second series 29 patients with 10 deaths (34%). The greatest single factor contributing to this reduction in mortality was the introduction of antibiotic therapy. None of the deaths in the second period was due to operative spread of infection.

In the first period pulmonary sepsis was the primary cause of brain abscess in 10 cases, the number of deaths from secondary brain abscess being 9. In the second period no case of brain abscess was thought to be secondary to infection in the lung or pleural space, suggesting that more skilful surgical treatment of lung sepsis and bronchiectasis, in addition to antibiotic therapy, had reduced the neurosurgical complications. Early operation, either aspiration or, under certain circumstances, excision, prevented in many cases the complications consequent upon rupture of the abscess into the cerebral ventricles or subarachnoid space.

The authors point out, however, that death from the effects of increased intracranial pressure occurs all too frequently. Earlier reference to a neurosurgical unit of any patient in whom a brain abscess is suspected would help to reduce still further the mortality from this cause. *J. V. Crawford*

1116. **The Treatment of Intracranial and Cranial Suppuration with Reference to the Local and Systemic Use of Bacitracin**
P. TENG and F. L. MELENEY. *Surgery* [*Surgery*] **33**, 321–332, March, 1953. 28 refs.

In 1951 the authors described the results obtained with bacitracin in the treatment of 61 patients with neurosurgical infections (*Surg. Gynec. Obstet.*, **92**, 53; *Abstracts of World Surgery*, 1951, **10**, 33). In the present paper a further 14 cases, similarly treated, are reported, including 7 cases of intracranial suppuration (3 of brain abscess, 3 of septic meningitis, and 1 of subdural empyema associated with an intracerebral abscess) and 4 cases of infected craniotomy wound, in 3 of which osteomyelitis of the skull developed. These 11 patients received bacitracin locally or by intrathecal, intracerebral, or intraventricular injection, with or without an intra-

muscular injection of the drug. There was one death in the series, from gastrointestinal and pulmonary complications. Bacitracin was given as a prophylactic to 3 patients, 2 with acute postoperative aseptic meningitis and 1 with a compound fracture of the skull with cerebral fungation. The antibiotic was given intrathecally in the first 2 cases and intracerebrally in the third.

Application of bacitracin " directly into and on the surface of the nervous system " produced no ill-effects. In the authors' view this lack of toxicity coupled with the fact that the commoner organisms causing neurological infections are sensitive to bacitracin make it the antibiotic of choice in such cases. [Little bacteriological detail is given in this paper, but it is mentioned that 97·3% of strains of coagulase-positive *Staphylococcus aureus* were sensitive to bacitracin, which fact alone makes this antibiotic a most useful addition to therapy.]

J. V. Crawford

CEREBRAL TUMOURS

1117. **Tumours of the Posterior Portion of the Third Ventricle**

R. W. RAND and L. J. LEMMEN. *Journal of Neurosurgery* [*J. Neurosurg.*] **10**, 1–18, Jan., 1953. 8 figs., 26 refs.

A review is presented of 32 cases of tumour in the posterior portion of the third ventricle and one case of ectopic pinealoma in the anterior third ventricle studied during the years 1930–51 at the University Hospital, Ann Arbor, Michigan. Of these, the diagnosis was confirmed histologically in 19, clinical and ventriculographic findings being relied on in the remainder. The majority of the patients were male, and although the average age was 21 years, 18 of them were under 16.

The primary clinical features were those of raised intracranial pressure from obstruction of the Sylvian aqueduct. Disturbance of ocular movement was common in the later stages. Loss of upward conjugate gaze was common, but disturbances of downward gaze and of pupillary size and reaction were also found. Cerebellar dysfunction was noted in 11 cases and nystagmus in 9. Endocrine and hypothalamic upsets were observed, but no patient developed precocious puberty. The anatomical basis of these clinical features is discussed. In most cases radiographs of the skull showed an abnormal picture with pressure changes in the sellar region and solid or scattered calcification in the pineal region. In most cases, too, ventriculography showed blockage of the aqueduct and obliteration of the suprapineal recess; in a few cases the foramina of Munro were also obstructed. In the 19 cases in which histological examination was made this disclosed a pinealoma in 9, a pinealoblastoma in 5, a teratoma in 4, and a glioma in one. All tumours were considered to have arisen either from the pineal body or from the midline structures in the posterior wall of the third ventricle.

Reports of 4 of the cases are included. In 2 of these the primary lesion was an ectopic tumour of pineal type in the region of the anterior part of the third ventricle and visual pathways. Operative treatment was directed to the tumour in 17 cases, but the operative mortality was heavy (70%); for this reason the authors advise palliative ventriculostomy followed by irradiation as the treatment of choice.

Brodie Hughes

1118. **The High Surgical Mortality in Cases of Chromophobe Adenoma of Abnormal Symptomatology. Prognostic Significance of Homonymous Lateral Hemianopia.** (La fragilité opératoire des malades atteints d'adénome chromophobe de symptomatologie anormale. Valeur pronostique de l'hémianopsie latérale homonyme)

D. PETIT-DUTAILLIS, J. CHAVANY, and G. GUIOT. *Presse médicale* [*Presse méd.*] **61**, 341–343, March 11, 1953.

In this study from the Neurosurgical Clinic of the Hôpital de la Pitié, Paris, an examination, based upon a detailed study of 3 cases, is made of the operative risk in the treatment of chromophobe adenomata. Though the physical resistance of these 3 patients was vastly different, they were alike in an identical susceptibility to operative interference, and the point is made that in each of them either atypical symptoms were present or the course of the disease was abnormal.

Normally in such cases pressure signs are preceded by those of glandular deficiency, which may be indefinite and so liable to be overlooked; these signs may develop over a course of many years, with periods of arrest and relapse. There is, in fact, no unity of time, and this may give a misleading impression regarding the severity of the condition. It is only later that the picture is dominated by the classical bitemporal hemianopia, supported by characteristic radiographic appearances in the sella—signs which tend to overshadow disturbances in the functions of sleep and heat regulation and the metabolism of water which are associated with pressure on the diencephalon. In cases which follow the normal course the hemianopia is always bitemporal, the pressure signs are local, and there is no cortical reaction. Though total blindness may develop later, the bitemporal stage is not by-passed. There is, in fact, a unity of place.

It is cases in which this unity is not present that are attended with grave surgical risk. In the first case reported here there was an unusually long history of tumour of the hypophysis (verified in 1929), but the patient (a man then aged 35) was able to continue work until 1947, when an attack of aphasia, complete but lasting for only 3 days, occurred. Even then the patient refused operation. It was only in 1950 that this was undertaken on the insistence of his relatives, on account of his increasing lassitude, apathy, and somnolence and a general slowing down of the mental processes. He did not survive the removal of an enormous chromophobe adenoma.

In the other 2 cases reported, the abnormal sign was a homonymous lateral hemianopia, which had appeared only a short time before the operation. In the first of these its appearance had been preceded by various regressive visual accidents, more suggestive of aneurysm than of adenoma. In the other case it was associated with intense, continuous, left-sided headache and a central scotoma, but preceded by none of the usual endocrine symptoms or signs of pressure on the diencephalon.

There was, in fact, unity neither of time nor of place. Neither of these patients survived operation, in spite of their being apparently in good physical condition.

From these observations the authors draw the following conclusions: (1) the appearance of either aphasia or a homonymous lateral hemianopia is presumptive evidence of a tumour larger, on account of its supraclinoid extension, than would be suggested radiographically, and carrying an increased operative risk; (2) that operation should not be delayed until the terminal stage has been reached; and (3) that a very limited operation is advisable in the first instance, even if it means further intervention at a later date. *D. P. McDonald*

PERIPHERAL NERVES

1119. **Electron Micrographs of Motor End-plates**
H. W. Beams and T. C. Evans. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **82**, 344–346, Feb., 1953. 7 figs., 5 refs.

Preliminary observations on the motor end-plates as shown by the electron microscope are reported in this paper from the State University of Iowa. Examination of the motor end-plates in the intercostal muscles of the rat revealed prolongation of the Z membranes of the muscle into the sole-plate sarcoplasm. This appeared to indicate a closer association of the Z membranes of the muscle fibre with the nerve endings than is generally thought to be the case. The authors consider, however, that this association does not amount to structural continuity, but rather that the relationship resembles that existing at a synapse. *L. Crome*

1120. **Polyradiculitis Cervicalis Infectiosa (Myalgia Nuchae Epidemica).** [In English]
J. Ström. *Acta medica Scandinavica* [*Acta med. scand.*] **144**, 408–429, Feb. 28, 1953. 28 refs.

During the 6-year period 1946–52, 72 patients were admitted to the Hospital for Contagious Diseases, Stockholm, with pain at the back of the head and neck, restriction of neck movement, headache, malaise and vomiting, raised temperature, and neck stiffness—a syndrome suggestive of incipient poliomyelitis or serous meningitis, while the myalgia resembled that of Bornholm disease. The period of incubation for the condition was between 1 and 6 days, and personal contact appeared to play an important part in transmission of the illness. In 7 cases a skin eruption appeared which was, however, transitory in 5 cases. Examination of the cerebrospinal fluid revealed only a slight increase in the protein content, and the cell count was within normal limits. Some cases showed elevation of the erythrocyte sedimentation rate; the blood picture varied, but tended to be leucopenic. The disease ran an acute course, ranging from 4 to 19 days in duration. Immunity was not acquired and recurrence was not infrequent. Treatment, which was symptomatic and directed only to securing adequate analgesia for relief of the often intense pain, varied from case to case. Infiltration with 0·5% procaine at the site of greatest tenderness was found to be helpful.

The author discusses the pathogenesis at length, and is led to the conclusion that the site of affection is the nerve roots, particularly as biopsy of tender muscle has in 9 of the cases revealed no abnormality. He suggests that the condition should be named " polyradiculitis cervicalis infectiosa ", and considers it to be either a viral or a bacterial infection—more probably the former—by an as yet unidentified organism. A Coxsackie virus, which was sought in 15 cases, could not be demonstrated. *L. A. Liversedge*

1121. **Traumatic Ulnar Neuritis.** (Die traumatische Neuritis des Nervus ulnaris. Eine Analyse 73 von operierten Fällen)
H. Nigst. *Helvetica chirurgica acta* [*Helv. chir. Acta*] **20**, 37–51, March, 1953. 2 figs., 10 refs.

SPINAL CORD

1122. **The Interrelation of Trauma and Cervical Spondylosis in Compression of the Cervical Cord**
Charles Symonds. *Lancet* [*Lancet*] **1**, 451–454, March 7, 1953. 6 refs.

Cervical spondylosis with disk degeneration and protrusion is being increasingly recognized as a cause of cervical cord compression. In one type of case compression of the cord occurs without any preceding injury to the head or neck; in a second type it occurs a long time after an injury; and in a third type, cervical spondylosis is present and injury precipitates the cervical cord symptoms. It is with this third type of case that the present paper, from Guy's Hospital and the National Hospital, Queen Square, London, is particularly concerned. It is pointed out that either over-flexion or over-extension of the cervical spine may be the causal injury. Injury by hyperextension of the cervical spine may occur when a patient is under general anaesthesia, and special care should be taken to avoid this if there is any indication of the presence of cervical spondylosis. A number of illustrative case histories are included in the paper. *J. W. Aldren Turner*

1123. **Diagnostic Lumbar Disk Puncture. Clinical Review and Analysis of Sixty-seven Cases**
L. Walk. *Archives of Surgery* [*Arch. Surg. (Chicago)*] **66**, 232–243, Feb., 1953. 7 figs., 9 refs.

At the Central Hospital, Eskilstuna, Sweden, the radiological findings in 67 patients examined by lumbar-disk puncture were assessed clinically. Lindblom's technique, which avoids exposure of the radiologist's hands to the rays, was modified as follows. Instead of introducing the needle under fluoroscopic control, the posterior arch of the vertebra was localized by bone contact with the needle, which had to be introduced just below the arch. A double needle was used, the position being checked on lateral radiographs. The inner needle was introduced to the depth of the nucleus, and 0·5 to 2 ml. of a mixture containing 2 ml. of a 35% solution of diodone

with 0·5 ml. of a 5% solution of procaine was injected. The presence and distribution of the pain on injection were noted.

The 67 cases, with a total of 98 disks examined, were divided into 4 groups: (1) normal disks; (2) disks with no, or only slight, deformity of the nucleus, a posterior or lateral rupture, and spread of the medium; (3) degenerated disks with a broad cavity instead of the nucleus; and (4) degenerated disks as in (3), but with a posterior or lateral rupture and spread of the medium.

It is stated that the " ordinary myelographic appearance of a disk prolapse is usually found in rupture, with tissue particles in the spreading contrast, or with a posterior bulging of the edges of the rupture; it may even occur in degenerated bulging disks without rupture. Two types of prolapse are thus differentiated on disk puncture, which apparently is not known in the literature ". Of the lateral prolapses, invisible in the myelogram, disk puncture visualizes those of Groups 2 and 4, with lateral tissue particles. Prolapses of Group 3, if too lateral to cause any impression in the myelogram, will remain undetected even on disk puncture.

Discussing the clinical findings, the author states that pain on disk injection appears to be independent of the duration of the disease. Pain on coughing is more frequent in disk rupture than in degenerated disks without rupture. A strongly positive Lasègue sign occurs oftener in disks with rupture than in those without. In simple degeneration of the disk this sign occurs less frequently, and in simple rupture it usually disappears in a few months. Numbness is less frequent in disks with rupture.

The pain produced by injection is not in itself an indication for surgical treatment. In rupture with spread of the medium, surgery is indicated only if tissue particles are found in the medium or if there is bulging of the edges of the rupture. If these conditions are absent, negative findings at operation are to be expected, even if there has been radiating pain on injection. In verified disk prolapse, puncture may demonstrate a degenerated disk but no rupture—such are the degenerated disks with local posterior bulging (concealed disks) of Group 3. *D. P. McDonald*

1124. **A Critical Study of the Surgical Treatment of Lumbo-sciatic Pain; Statistical Analysis of 1,000 Cases.** (Étude critique du traitement chirurgical de la lombo-sciatique; d'après l'étude statistique de 1,000 cas opérés) J. GUILLAUME and P. JANNY. *Presse médicale* [*Presse méd.*] **61**, 172–174, Feb. 11, 1953.

This critical study from the neurosurgical service of the Salpêtrière Hospital, Paris, is based upon the statistics of 1,012 cases of lumbo-sciatic pain operated on between 1943 and 1951. The authors first draw attention to the great divergence in the figures reported by other French workers regarding the frequency of disk hernia discovered at operation, which have varied from 44% to 83%. Such a divergence naturally gives rise to very different attitudes towards the surgical treatment of lumbo-sacral pain, the one side contenting themselves with removal of the offending disk, the other practising a lumbo-sacral arthrodesis, either primarily when the disk lesion does not appear to be a sufficient cause of the symptoms, or secondarily when, after removal of the disk, a residual lumbalgia is anticipated. One authority (Merle d'Aubigné) even goes so far as to perform a primary arthrodesis in nearly 75% of his cases. Any discussion, therefore, on the treatment of lumbo-sacral pain due to a displaced disk is liable to be coloured by some individual pathogenic concept, or some particular surgical technique, and it is for that reason that the present authors have submitted to the rigour of a mathematical analysis a sufficient number of cases upon which to base a valid assessment.

In the present series they are concerned exclusively with cases of ordinary lumbo-sacral pain of diskal origin, in 94% of which hernia of a disk was found at operation. Removal of the disk sufficiently to free the nerve roots is the most obvious and effective treatment, and in 90% of cases where such freeing of the roots was achieved a cure resulted at the cost of an interference of no great severity (no death occurred in the whole series), and a period of immobilization which did not in any instance exceed a few weeks.

Admittedly, many herniated disks are difficult to expose, by reason of a situation abnormally high or abnormally lateral, but the only way to make certain that an intervertebral space is not the seat of disk protrusion is to expose completely the corresponding root from its emergence from the dural sac to its ganglionic enlargement, and not to hesitate to explore the spaces above and below, if necessary in two stages. The present authors met the typical, rounded, protruding diskal nodule, over which the root is tautly stretched, in 75% of their cases, and they are convinced that a rigorous and methodical search would disclose a lesion of the disk in the great majority of cases of lumbo-sacral pain. In only 61 cases (6% of the whole series) could no disk lesion be found.

The results of operation were as follows: " perfect ", 34·3%; " good ", 52%; with residual pain less severe than the original, but still to a certain extent causing diminution in activity, 7·2%; no benefit or worse, 6·5%. It is interesting to note that 90% of these patients were in hospital for less than 12 days, and after a rapid convalescence were restored to normal activity within 2 months. A small number of patients had residual chronic lumbalgia, which necessitated a change in occupation, or even cessation of work. In 2·5% the improvement was transitory with severe relapse, but the number of cases which could be described as complete failures was only 4·1% of the whole series. In view of these satisfactory results, the authors are confirmed in their belief that arthrodesis should be reserved for the relatively few cases in which more conservative methods have failed to give relief—especially for severe residual lumbalgia. The disadvantages of arthrodesis are numerous, and include the injudicious imposition of a graft upon a protruded disk which has remained unrecognized because it had not been properly sought for. For cases of true spondylolisthesis fixation is the procedure of choice, though even there, in a series of 7 such cases, the authors found a diskal hernia in 5. *D. P. McDonald*

Psychiatry

1125. **Disturbances of the Body-scheme after Administration of " LSD 25 ".** (Körperschemastörungen bei LSD 25)
O. H. Arnold and H. Hoff. *Wiener Zeitschrift für Nervenheilkunde* [*Wien. Z. Nervenheilk.*] **6**, 259–274, 1953. 2 figs., 29 refs.

The authors, having observed that after administration of " LSD 25 " 90% of normal subjects showed alterations in those parts of the personality which are usually regarded as the sphere of the " self ", proceeded to investigate the particular alterations in the body-scheme, in view of the undoubtedly important role which the latter plays in the awareness of the self. They point out that, apart from the sensations of smell and taste, sight and hearing, awareness of the body is derived from the interplay of three groups of sensations—namely, those from the surface of the body, those from the kinaesthetic and vestibular apparatus, and those from the internal organs.

Details of 5 cases studied at the University Psychiatric Clinic, Vienna, are given, together with the subjects' descriptions of the changes they experienced in their appreciation of their own bodies and their relationship to external space. So far as alterations in respect of the body-scheme were concerned, these were remarkably similar in all the subjects, and consisted of various distortions of bodily experience which produced a result that could be represented diagrammatically in a sketch, which was then seen to have a remarkable similarity to the mannikin constructed by Penfield to illustrate the bodily representation in the motor cortex. It consists of a large head, with exaggerated mouth and accentuation of the nose and chin, perched on a globular, dwarfish body from which spring hands and feet without any, or with only very spindly, intervening limbs. The hands have a greatly enlarged thumb, a long index finger, and a disproportionately long little finger. At the same time the faces of other people appeared to most of the subjects to take on an acromegaloid character, and portraits of women appeared like those of old hags. One subject had the feeling of being changed into a wolf and felt compelled to snarl at people, and 2 patients with phantom limbs were quite convinced, under the influence of LSD 25, that their amputated limbs were back in place and quite normal. Changes in sensation from the internal organs —such as " confluence of the stomach, heart, and lungs", or " numbness in the digestive organs "—were described, which were quite similar to the complaints of many schizophrenics. The awareness of a boundary between the subject's body and the external world became clouded in one subject.

In drawing attention to the resemblance between the body-scheme, as described by the subjects, and Penfield's mannikin, the authors recall the rather similar result which appears in spontaneous drawings of human figures made by children, and suggest that the effect of LSD 25, in that general sphere of the personality concerned with awareness of the self, is to cause a descent to an ontogenetically more primitive level. They suggest that clinical observations on this dedifferentiating effect of LSD 25 may reveal some clues to the functional organization of the somatopsyche through the changes wrought in the body-scheme and in the awareness of the bodily status, both of which constitute aspects of the somatopsyche of the first importance.

J. B. Stanton

TREATMENT

1126. **The Dream-life in Leucotomized Patients.** (Das Traumleben der Leukotomierten)
R. Schindler. *Wiener Zeitschrift für Nervenheilkunde* [*Wien. Z. Nervenheilk.*] **6**, 330–334, 1953. 8 refs.

The effect of leucotomy on the dreaming habits of 150 patients was investigated at the University Psychiatric Clinic, Vienna, and found to follow a fairly constant pattern. As a rule, patients who previously had had fairly vivid dreams or nightmares experienced an absence of dreaming after leucotomy, which lasted for several months or even over a year. After this gap, dreaming started again, but the content was more superficial than before the operation, and was composed of more " daytime residues " and more primitive wish-fulfilments. In some 11% of patients the capacity for dreaming seemed unaffected by leucotomy, and the author draws attention to the fact that these fall amongst the 25% in whom the operation also produced little clinical effect. He suggests that more of this group would possibly have shown continuation of dreaming if rapport with the patients had been good enough for this information to be elicited.

The usual time for the re-establishment of dreaming is the point when the postoperative period of affective lability begins to yield to that of affective stability. If dreaming returns during the labile phase, as it did in 8% of the author's cases, a relapse in the clinical condition is to be expected within the next 2 weeks. As to the origin of the postleucotomy interval in dreaming, the author does not think this lies in the greater depth of sleep, or in greater difficulty in remembering the dreams, but in a diminishing of affective tension, which precludes any vivid representation of the dream-world. In apparent confirmation of this are the statements of 2 of the patients that they felt as if they had had a dream but there had been nothing to see. The author surmises that the cutting of fronto-thalamic connexions at leucotomy may lower the affective significance of past events so that affective echoes of the day are no longer likely to threaten sleep. With the building up of a new functional organi-

zation at the end of the postoperative period formed elements are again experienced in dreams, but these are less rich than formerly in memories and elements from the past.

From the clinical point of view the author regards the dreaming capacity as a useful prognostic guide to the success of a leucotomy. If there is no interruption of dreaming at all, the operation has probably been a failure; if dreaming reappears too early, while the patient is still in the stage of affective lability, a relapse threatens and the author regards this as an indication for giving electric convulsion therapy. If dreaming does not reappear until the stage of affective stabilization is reached, then the operation has probably been a success, and the reappearance of dreaming may be a valuable indication of the entry into this last postoperative phase.

J. B. Stanton

1127. **The Changes in Thiamine Requirements during Treatment with Prolonged Sleep.** (Изменение потребности в тиамине (витамин B_1) при лечении длительным сном)

L. K. Bauman, E. S. Prokhorova, and V. N. Kazmina. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **53**, 42–45, Jan., 1953. 3 figs., 14 refs.

The estimation of thiamine in the urine of patients undergoing sleep therapy has shown its excretion to be diminished, indicating diminished utilization in the body. This finding is the reverse of that observed in normal sleep. It was therefore decided to add thiamine to the glucose given to patients undergoing such treatment. This proved satisfactory in mitigating certain of the toxic effects of the barbiturate drugs used for maintenance of therapeutic sleep.

L. Crome

1128. **New Variants of Sleep Therapy in Psychiatric Cases.** (О новых вариантах лечения сном психически больных)

V. E. Galenko. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **53**, 58–66, Jan., 1953. 37 refs.

Encouraging results were obtained by the combined use of " barbamyl ", sodium bromide, 33% alcohol, and 1% glutamic acid in the induction and maintenance of prolonged sleep. An essential condition for success was enforcement of silence, the use of small wards, and the careful adjustment of the amount and optimal combination of the above drugs for each individual case. The treatment was used for various psychiatric disorders.

L. Crome

1129. **Combined Method of Treatment of Schizophrenia with Sleep and Insulin.** (Комбинированный метод лечения больных шизофренней сном и инсулином)

Y. A. Pavorinski. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **53**, 67–71, Jan., 1953. 2 figs., 2 refs.

It is stated that the following method was used with some success in the treatment of schizophrenia. Small doses of insulin, 4 to 8 units, were given daily at first, and then increased by 4 to 8 units a day until the onset of the first coma, which was terminated immediately by the administration of glucose. The patients then received hypnotic doses of amylobarbitone sodium during the same day, and for a further 24 hours. After this the insulin treatment was resumed until a pre-comatose or comatose state again resulted and was again terminated by glucose. These cycles were continued until the patient had 15 attacks of coma or pre-coma and 200 to 300 hours of sleep.

L. Crome

1130. **Effect of Prefrontal Lobotomy on Intellectual Functioning in Chronic Schizophrenia**

P. B. A. Struckett. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **69**, 293–304, March, 1953. 5 figs., 15 refs.

The effect of prefrontal leucotomy upon intellectual functioning, as measured by psychometric tests, was evaluated in 26 chronic schizophrenic patients at the Westminster Hospital, London, Ontario. The results of tests carried out before operation were compared with those obtained at intervals of 3 weeks, 3 months, 6 months, and one year afterwards, the tests of intellectual functioning being the Wechsler–Bellevue Intelligence Scale, Wechsler Memory Scale, Benton Visual Retention Test, and Raven's Progressive Matrices. The most reliable test was the Wechsler–Bellevue Intelligence Scale, the Matrices and Wechsler Memory Scale being considered the next most reliable.

Examination of the results indicated that all four tests revealed a decrease in intellectual functioning 3 weeks after operation, followed by a gradual increase until, at 6 months, the intellectual capacity equalled that found before operation, with a further increase demonstrable at the end of the one-year period. For 11 of the patients, the Army (" pre-psychotic ") test scores were available, and a comparison of these with the results of the tests after leucotomy showed that the latter not only exceeded the pre-operative values after a suitable interval, but tended to equal the " pre-psychotic " scores. The author suggests that the remaining slight deficit in intellectual functioning is not due entirely to operation but may be caused, in part, by the deteriorating effect of the psychosis. She points out that while it would be rash to assert that prefrontal leucotomy has no effect on intellectual functioning, nevertheless, after 6 months, objective psychometric tests revealed no decrease in these functions as tested.

[The importance of allowing a sufficient period to elapse after operation before assessing any change in intellectual functioning is apparent.] *J. B. Stanton*

1131. **The Treatment of Delirium Tremens.** (Sulla terapia del delirium tremens)

P. Dogliani. *Cervello* [*Cervello*] **29**, 265–277, July 15, 1953. 20 refs.

1132. **Thiamylal in Electroconvulsive Therapy and Significance in Analysis of Seizure Mechanisms**

R. S. Green and R. Leiser. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **69**, 737–742, June, 1953. 10 refs.

Dermatology

1133. **Aqueous Solutions of Sodium Propionate with Chlorophyll as a Therapeutic Agent**
S. M. PECK, E. F. TRAUB, and H. J. SPOOR. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **67**, 263–277, March, 1953. 6 figs., 28 refs.

In an investigation at the New York Medical College a series of more than 100 cases with a great variety of skin lesions were treated with an aqueous solution of sodium propionate to which chlorophyll was added to combat the unpleasant odour. In this it was successful, and in addition it was thought that the therapeutic efficacy of the mixture was enhanced. The solution was applied variously as a wet dressing, a mouth-wash, a vaginal douche, and a foot-bath. It is bacteriostatic and fungistatic, promotes healing, and has marked antipruritic properties; at the same time no toxic effects were noted and the index of sensitization was low.

Of the various skin conditions treated, seborrhoeic eczema showed the greatest improvement. In neurodermatitis, acute contact dermatitis, and rectal eczema there was marked amelioration of pruritus, though the underlying condition was not affected in the last two. Used as a mouth-wash, the solution gave symptomatic relief in such diverse lesions as lichen planus, aphthous stomatitis, pemphigus vulgaris of the mouth, and leucoplakia. It appears thus to be beneficial wherever wet dressings are indicated, particularly when infection and irritation are troublesome. *G. W. Csonka*

1134. **Diseases Related to Light Sensitivity**
B. M. KESTEN and M. SLATKIN. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **67**, 284–301, March, 1953. 2 figs., 43 refs.

1135. **Observations on the Persistence of Skin Sensitivity with Reference to Nickel Eczema**
J. K. MORGAN. *British Journal of Dermatology* [*Brit. J. Derm.*] **65**, 84–94, March, 1953. 44 refs.

Over a period of 10 years 58 patients with contact dermatitis due to sensitivity to nickel were seen at Leeds General Infirmary. In 55 of the patients the primary site of the eczematous reaction was the skin in contact with nickel-plated suspenders; in 31 there was secondary eczema at other sites as well. All but one of the patients were traced and re-examined 1½ to 11½ years later. Patch tests were performed at the original examination and subsequently with one drop of 10% nickel sulphate solution on lint. Sensitivity persisted in 31 patients as shown by the presence of contact dermatitis on exposure and freedom from dermatitis in the absence of exposure. Negative results to repeated patch tests were obtained in 23 patients, though 18 of them continued to have eczema. In 9 patients, whose sensitivity did not last more than 18 months, the nickel dermatitis was probably only an incident in the course of a series of eczematous eruptions. The author considers that prognosis depends more on the patient's constitutional background than on the nature of the specific agent. Attention is drawn to the possibility of nickel sensitivity arising as the result of handling nickel coins. *E. Lipman Cohen*

1136. **Systemic Disturbances in Recalcitrant *Trichophyton rubrum* (*purpureum*) Infections. Studies and Short Report on Therapeutic Experiments**
S. ROTHMAN. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **67**, 239–246, March, 1953. 3 figs., 20 refs.

In an investigation at the University of Chicago it was found that of 20 cases of treatment-resistant *Trichophyton rubrum* infection the glucose tolerance curve was abnormally flat or low in 13. According to the author, 112 mg. per 100 ml. is the lowest normal " peak " recorded. In 8 of the present series there was a peak value of 105 mg. per 100 ml. or less, and 5 showed a less pronounced increase in glucose tolerance with a peak value of 122 mg. per 100 ml. or less. No endocrine disorders were present to account for these results, and it is postulated that if the glucose content of the skin is low the fungus adapts itself to metabolize substances other than glucose and thereby acquire greater resistance to fungistatic agents which primarily inhibit carbohydrate utilization. To produce alimentary hyperglycaemia, thyroid was given, with equivocal results on the skin infection. When combined, however, with local lithium bromide treatment to the nails, palms, and soles, together with local glucose spray, good results were recorded in 9 very resistant cases after several months of treatment. *G. W. Csonka*

1137. **Generalized *Trichophyton rubrum* Infection Associated with Systemic Lymphoblastoma. Report of Three Cases**
G. M. LEWIS, M. E. HOPPER, and M. J. SCOTT. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **67**, 247–262, March, 1953. 6 figs., 15 refs.

From the New York Hospital and Cornell University Medical College are reported 3 cases of generalized cutaneous infection with *Trichophyton rubrum* seen in patients with lymphoblastoma (lymphatic leukaemia, lymphosarcoma, and monocytic leukaemia respectively). The coexistence of two rather uncommon diseases was not thought to be a chance association, though the basis of such linkage is not known. The possibility that the systemic disease lowers resistance and thus predisposes to the active invasion of *T. rubrum* is considered. It is suggested that the similarity of *T. rubrum* infection to psoriasis, mycosis fungoides, dermatitis herpetiformis, and neurodermatitis may lead to errors in diagnosis, especially if the atypical forms of *T. rubrum* infection are not studied mycologically. *G. W. Csonka*

Paediatrics

1138. **Idiopathic Celiac Disease—I. Mode of Onset and Diagnosis**
D. H. ANDERSEN and P. A. DI SANT'AGNESE. *Pediatrics* [*Pediatrics*] **11**, 207–223, March, 1953. 1 fig., 24 refs.

According to the authors, who studied 58 cases of idiopathic coeliac disease at the Babies Hospital, New York City, the " coeliac triad " consists of diarrhoea with loose, bulky stools, weight loss, and abdominal enlargement; this, they say, suggests the diagnosis, which requires confirmation by one or more laboratory tests. " No single test is pathognomonic of the disease and diagnosis should be based on the clinical and laboratory picture as a whole." All the 58 cases studied fulfilled the following criteria: (1) the patient was between the ages of 6 months and 5 years at the time of study; (2) there was persistent or recurrent diarrhoea with large, foul, bulky stools; (3) steatorrhoea had been present during the severe phase of the illness; (4) there was abdominal enlargement; (5) the muscles were small, weak, and flabby; (6) weight had at some stage been two standards or more below the normal mean for the age; (7) the patient failed to thrive on a normal diet and improved on a diet designed for coeliac disease; (8) the duodenal juice contained a normal concentration of trypsin; and (9) no anatomical or bacteriological cause for the diarrhoea could be found.

All 58 cases were of moderate degree. In the majority of them (36) the diagnosis was made between the 6th and 15th months of age, and in only one case before 6 months. The appearance of one or other symptom of the " coeliac triad " before 3 months of age was, however, noted in 26 cases, and this suggested to the authors that there has been an earlier onset of the disease in the U.S.A. in recent years, probably due to the adoption of artificial feeding at an earlier age. Their study of the influence of breast-feeding on coeliac disease leads them to believe that breast-feeding for more than 2 and up to 6 months may retard the first appearance of diarrhoea, but not the later development of the disease.

The laboratory tests are fully explained and their results given. The concentration of trypsin in the duodenal juice was within normal limits, thus affording a valuable means of differentiation between coeliac disease and fibrocystic disease of the pancreas. The lipase level was also normal. The amylase–trypsin ratio, which the authors claim to be of more value in diagnosis than the amylase level alone, was abnormally low in 52 of the cases. The results of glucose tolerance tests (oral) varied, and these tests are regarded by the authors as unreliable in that normal blood sugar curves were obtained in 13 out of 34 cases. Low serum protein levels were found to be useful, not in diagnosis, but in giving timely warning of a " coeliac crisis " (dehydration and acidosis). Faecal fat determinations, by chemical methods or by microscopical examination, gave raised figures in every case, and clinical improvement was associated with a fall in the stool fat content. A negative correlation was found between serum carotene and faecal fat levels, the former being low when fat in the stool was high, and vice versa.

The authors express the view that in idiopathic coeliac disease " evidence has been accumulating that there is . . . a hereditary constitutional defect in metabolism or physiology which persists after the clinical manifestations of the severe illness have disappeared ".

Charles McNeil

1139. **Idiopathic Celiac Disease—II. Course and Prognosis**
P. A. DI SANT'AGNESE. *Pediatrics* [*Pediatrics*] **11**, 224–237, March, 1953. 4 figs., 15 refs.

At the Babies Hospital, New York City, 23 patients who had received treatment for coeliac disease, 20 of whom are included among the 58 cases described above [Abstract 1138], were re-examined 3 to 11 years after their admission to hospital. A general description of the course of illness and prognosis in the whole series of 58 cases is given. There were 3 deaths in hospital. Episodes of " crisis " (sudden dehydration and acidosis) occurred in 35 of the cases. The early phase of improvement was often rapid and lasted 6 to 24 months, and this was followed by a slower phase marked by an occasional relapse, with return of the diarrhoea, often associated with upper respiratory infection and dietetic errors.

Of the 23 patients who returned to hospital for clinical assessment and laboratory tests, the great majority were reported to be healthy and active. In only 2 cases were growth and development seriously retarded, and in these 2 cases and also 2 others the patient's condition was regarded as unsatisfactory. The general picture of good nutrition, growth, and activity was, however, accompanied by abnormal laboratory and radiological findings similar to those obtained during the active stage of the disease, indicating that in most cases there was still impairment of fat absorption as shown by excess of fat in the stools, low level or absence of serum carotene, and a poor response to the vitamin-A test.

The author concludes from these and other abnormal findings that these children, who had apparently recovered from coeliac disease and were leading normal lives, were still in what he regards as the latent phase of the disease.

Charles McNeil

1140. **Terramycin in the Treatment of Infantile Diarrhoea**
R. A. SHANKS. *Glasgow Medical Journal* [*Glasg. med. J.*] **34**, 48–51, Feb., 1953. 6 refs.

Terramycin was used in the treatment of acute non-specific infantile diarrhoea or gastro-enteritis in addition to the routine treatment of starvation and rehydration. Comparison with the results obtained with aureomycin

and chloramphenicol and a combination of sulphonamide and penicillin revealed no significant difference in effect.

It is concluded that some anti-bacterial adjuvant is useful without being specific and that terramycin is a simple and effective drug for this purpose.—[Author's summary.]

1141. **A Case of Periarteritis Nodosa in a Child.** (Случай узелкового периартериита в детском возрасте)

E. B. Voit and N. A. Denisova. *Педиатрия* (*Pediatriya*] No. 1, 62–66, Jan.–Feb., 1953. 4 figs.

A boy aged 12 was admitted to hospital after a fall while skiing, the diagnosis on admission being concussion and injury to the hip-joint. The patient's condition is described in detail. Before the accident he suffered from general debility, fatigue, headaches, and night sweats; while in hospital his condition gradually deteriorated and eventually a clinical diagnosis of acute nephritis with cardiac decompensation was made. The boy died 38 days after admission.

The pathological condition of the heart, liver, and kidneys was elucidated at necropsy, and is described. Histological examination revealed multiple lesions in the muscular layers of the small and medium-calibre arteries in the kidneys, liver, gall-bladder, pancreas, intestines, and heart. A diagnosis of periarteritis nodosa with definite characteristic changes in the arteries and the vasa vasorum was made. In addition, there was dilatation of the heart and hypertrophy of the left ventricle, bilateral pneumonia, partial obliteration of the pleural cavity, acute hyperplasia of the spleen with fibrosis of the capsule, and punctate haemorrhages in the mucous membranes and on the skin of the abdomen and chest.

The authors describe 3 further cases of nodular periarteritis in children (aged 10, 11, and 6 years) admitted to the hospital between 1941 and 1950, and review many other cases of periarteritis reported in the Russian literature, on which they make their own observations and comments. *H. W. Swann*

1142. **Purpura in Infants and Children. Its Natural History**

D. H. Clement and L. K. Diamond. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **85**, 259–278, March, 1953. 3 figs., 5 refs.

The authors discuss the causes of purpura and review 140 cases, with onset before the age of 12, treated at the Infants' and Children's Hospital, Boston, between 1936 and 1947. The ratio of non-thrombocytopenic to thrombocytopenic cases was 1 : 2, but this is attributed to the selection of in-patient cases for study.

The criteria for diagnosis are not fully defined, but it is stated that the non-thrombocytopenic cases were diagnosed on the basis of the clinical picture, platelet count, and tourniquet test, the last being positive in only 10%. About half the cases occurred before the age of 4, with a tendency to increased frequency again at 8. There was no significant sex difference, and thrombocytopenia tended to occur more often in winter. There was a family history of allergy in 25% of non-thrombocytopenic and in 30% of thrombocytopenic cases, and a history of personal allergy in 20% of non-thrombocytopenic and 15% of thrombocytopenic cases. In about two-thirds of the cases there was an associated acute infection, usually upper respiratory. Drugs were not implicated as a cause.

Investigation of the blood showed that the haemoglobin concentration and the erythrocyte, leucocyte, and differential counts were related to incidental factors such as haemorrhage or infection, but that eosinophilia was present in roughly one-quarter (34) of all the cases and was more marked in the thrombocytopenic group. The platelet count tended to be raised in the non-thrombocytopenic group. Clotting time was normal in both groups; bleeding time was, as a rule, normal in the non-thrombocytopenic group and prolonged, sometimes up to 30 minutes, in the thrombocytopenic cases. Splenomegaly was found in 13 of the 96 thrombocytopenic cases, but in only 2 was this marked.

The course of the non-thrombocytopenic cases was benign, although urinary abnormalities, in some cases associated with temporary evidence of impairment of renal function, were found in 12 cases. Of these cases 10 were anaphylactoid, with purpura, joint pains, and possibly abdominal pain or haematuria. The thrombocytopenic group (96 cases) showed a variable course: 33 patients were symptom-free in 6 weeks, 19 in a year or less, and the remainder showed variation in bleeding or bruising for as long as 15 years. There were 4 deaths, all in thrombocytopenic patients, death in 2 cases being ascribed to acute pneumonia and in one to nephritis and myocarditis.

It is concluded that thrombocytopenic purpura is often an acute, self-limited illness associated with antecedent infection.

[This article suffers from absence of definition of terms. It is to be regretted that Gairdner's (1943) review of Henoch–Schönlein disease (anaphylactoid purpura) is not referred to, as this applies to five-sixths of the non-thrombocytopenic group and, depending on definition, is not true purpura.] *H. Gordon*

1143. **Treatment of Neurogenic Urinary and Fecal Incontinence in Children**

R. E. Gross, G. W. Holcomb, and H. Swan. *Archives of Surgery* [*Arch. Surg.* (*Chicago*)] **66**, 143–154, Feb., 1953. 2 figs., 6 refs.

In this paper from the Children's Hospital (Harvard Medical School), Boston, an assessment is made of the remedial measures available in cases of anal and bladder incontinence due to congenital lumbo-sacral neural defects. It is stressed that although the incontinence is permanent and incurable in such cases and it is never possible to make these children normal, yet much can be done to make them less malodorous and more happy. The methods employed in 21 cases in children ranging from 4½ to 10 years of age are described.

In 4 of these the urine was diverted to the colon (which ended as a colostomy) giving a wet colostomy, while in 9 others an artificial bladder was constructed from a

segment of the sigmoid colon, one end of which was brought out as a stoma on the anterior abdominal wall. Though previously existing cutaneous lesions healed very promptly, both of these procedures brought problems of their own. The wet colostomy was difficult to handle, though the recent introduction of plastic colostomy bags—inexpensive and expendable—has made the problem less formidable. The sigmoid bladder in most cases provided a capacious receptacle, but in at least one case was liable to develop spasm with severe and intractable abdominal pain, after which urine would be shot out under great pressure. Moreover calcareous deposits tended to collect, either lying free within the lumen or adherent to the bowe lwall, from which they could with difficulty be dislodged; ulceration was not infrequent, and perforation occurred in one case on two occasions. From their experience in these 9 cases the authors are now convinced that, although the sigmoid bladder has certain advantages, its risks are too great and that it should no longer be used. They prefer a wet colostomy with such an appliance as a Rutzen bag, which can be attached to the abdominal wall over a bowel stoma, in all cases where urinary and faecal incontinence are so severe as to render it necessary to divert both streams away from the perineum.

In less severe cases, even with considerable laxity of the anal or bladder outlet, or of both, it is possible that spontaneous improvement may occur, and no radical diversionary operation should be carried out before the age of 3 to 4 years. It is seldom necessary to perform a colostomy for anal incontinence alone, and treatment should rather take the form of a constipating diet and a daily cleansing enema. In mild cases, urinary incontinence may be reduced with active exercise of the bladder sphincters, by which the child may become conscious of the shut-off mechanism. When it is essential to divert urine from the perineum, severance of the urethra, closure of the bladder outlet, and the establishment of a permanent suprapubic cystostomy are advised. The catheter may be clamped and released every 3 or 4 hours if the kidneys are in good condition; otherwise it may be connected with a rubber bag. In cases in which there is mild laxity of the bladder outlet, with constant dribbling, plication of the bladder sphincters, using a retropubic approach, is worth trying before more destructive surgery is attempted. But whatever treatment is adopted in these cases, expert supervision is required indefinitely. *D. P. McDonald*

1144. **Urinary Changes in Infections of the Urinary Tract in Childhood**

P. L. MASTERS. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **102**, 76–85, 1953. 7 refs.

Writing from the Evelina Hospital for Sick Children, London, the author attempts to assess the diagnostic value of simple examination of specimens of urine obtained without a catheter in cases of urinary-tract infection. Catheter specimens from girls and non-catheter specimens from boys were examined to determine the dividing line between normal and raised leucocyte and erythrocyte counts, these being made in a Fuchs–Rosenthal counting chamber, with the specific gravity of the urine adjusted to 1,020. The method is described in detail. He concludes that 10 leucocytes and 5 erythrocytes per c.mm. may be taken as the upper normal limit. In urinary infections the presence of leucocytes and bacteria is the decisive factor. Specimens were considered to be infected if they contained at least 200 leucocytes per c.mm., or if a 3-mm. loopful of urine gave a growth of at least 100 colonies of a potential pathogen. Of 120 non-catheter specimens of urine from girls and 128 from boys examined by these means, only 21 (18%) and 10 (8%) respectively gave doubtful results which had to be confirmed by the examination of catheter specimens.

Franz Heimann

1145. **Incidence of Gross Visual Defects due to Retrolental Fibroplasia**

E. R. SCHLESINGER and I. MCCAFFREY. *Pediatrics* [*Pediatrics*] **11**, 238–245, March, 1953. 9 refs.

The authors, who work in the New York State Department of Health, analysed the incidence of retrolental fibroplasia as observed to occur among the 296,430 infants born in the years 1948 and 1949 in New York State, excluding New York City. The investigation was confined to those babies who weighed less than 2,000 g. according to their birth certificate and who had survived for a period of 4 months, 3,667 such infants being found. Questionaries were sent to the parents asking, amongst other things, whether any defect in vision had been noted. Where no reply was obtained, personal approach was made by a public health nurse. Replies to a total of 3,377 were thus obtained, and where defective vision was reported, further information was sought from the family physician and from ophthalmological reports.

From this material 50 cases of retrolental fibroplasia were identified—an over-all incidence of 1·5% of those contacted. In babies weighing under 1,000 g. at birth the incidence was 15·9%; in those weighing 1,000 to 1,499 g., 4·3% and in those weighing 1,500 to 1,999 g., 0·7%. The incidence according to the length of gestation as recorded on the birth certificate was: for periods under 7 months, 7·6%; for 7 months' gestation, 1·9%; and for periods of 8 months and over, 0·3%. For babies of equal birth weight, the shorter the gestation period the higher the incidence appeared to be. Major complications of pregnancy were no more frequent in the mothers of those affected than in the mothers of babies of equal weight not affected. There was no seasonal incidence, though the numbers were too small to be significant statistically. A geographical variation in incidence was, however, noted throughout the State, but this correlated with a geographical variation in the incidence of the birth of babies of small weight.

The authors emphasize that by their method of investigation only babies with a severe degree of retrolental fibroplasia are discovered, cases in which there has been partial or complete recovery being missed, and that this should be borne in mind when comparing their figures with others obtained by different means.

H. G. Farquhar

Medical Genetics

1146. **Roentgenologic and Clinical Aspects of Hyperphalangism (Polyphalangism) and Brachydactylism. Hereditary Abnormal Segmentation of the Hand**
M. I. SHOUL and M. RITVO. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 274–278, Feb. 12, 1953. 6 figs., 24 refs.

The authors describe, from the Boston City Hospital, Massachusetts, 3 cases of malformation of the hands, of which 2 occurred in the same family—mother and daughter—and the third patient was the mother's cousin. The syndrome consisted of a hyperphalangism with 4 instead of the usual 3 phalanges in the middle finger and sometimes the index finger. The authors point out that in typical cases of this syndrome, whereas the index, middle, and little fingers are short and correspond in length to the thumbs, the ring finger is unusually long. Other congenital anomalies may be found in other parts of the body. Of the 3 patients described 2 were mentally retarded and one showed psychoneurotic symptoms.

According to the authors the aetiology of hyperphalangism is unknown; the condition is inherited as a dominant factor through successive generations.

Franz Heimann

1147. **Heredity and Rheumatic Fever. A Study of 462 Families Ascertained by an Affected Child and 51 Families Ascertained by an Affected Mother**
A. C. STEVENSON and E. A. CHEESEMAN. *Annals of Eugenics* [*Ann. Eugen. (Camb.)*] **17**, 177–210, Feb., 1953. 24 refs.

The familial incidence of rheumatic fever was studied at the Royal Belfast Hospital for Sick Children, the basis of the investigation being the case records of 462 patients (185 boys and 277 girls) attending the Rheumatic Clinic. A health visitor went to the home of each child at least once and took a detailed family history. If a member of the family had a history suggesting rheumatic fever, he or she was examined and the relevant hospital records were studied. (These details are set out in full in an appendix to the paper.)

It was found that when neither parent was affected the proportion of brothers of the patient who also had rheumatic fever was 18 out of 670 (3%) and of sisters 43 out of 652 (7%). When one parent was affected the proportions were 6 out of 132 (5%) and 17 out of 110 (15%) respectively. Assuming random sampling of sibships, the risk for the siblings, estimated by Haldane's method, was 8% with normal parents and 17% when one parent was affected. It is pointed out that these figures underestimate the total risk to the brothers and sisters, as many of these were still children; in 71 of the 188 affected parents and aunts the onset of the disease was after the age of 15. Only 1 of the 10 surviving pairs of twins was monozygotic and in this pair both children were affected. In the 9 dizygotic pairs the second twin was unaffected in each instance. Although the authors had no control series, the increased risk to the sibs where one parent was affected suggests that genetic factors to some extent control susceptibility to the disease.

C. O. Carter

1148. **The Heritage of Hypertension**
C. B. THOMAS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **224**, 367–376, Oct., 1952. 8 figs., 22 refs.

An attempt was made to determine the part played by genetic factors in the aetiology of hypertension by an investigation among medical students at the Johns Hopkins University. Diagnosis of hypertension in the parents was based on information obtained by the student in consultation with his parents, supplemented by sphygmomanometrical readings and reports from the family doctor. Hypertension was present in 61 (11·5%) and probably present in a further 25 (4·7%) of 532 parents. [No distinction is made between essential and other types of hypertension.]

Certain determinants of the supposed pre-hypertensive circulatory lability were studied in 84 students having one or both parents affected, and in 100 with both parents normotensive. The incidence of traits in the groups with and without affected parents respectively was: high resting blood pressure (120/80 mm. Hg or above) 31% and 20%; high resting heart rate (80 or over) 25% and 8%; positive cold pressor test (rise of 20 mm. Hg systolic and/or diastolic) 25% and 20%; overweight (20 lb. (9 kg.) or more above standard) 20% and 11%; transitory hypertension (150/90 mm. Hg or above) 15·5% and 9%; hyper-reactivity to exercise (pulse pressure rise of 42 mm. Hg and heart rate rise of 28 or more after exercise) 11·9% and 3%; and transitory tachycardia (100 beats a minute or above) 9% and 14%. Of 84 individuals with a history of parental hypertension, 33 had two or more traits, compared with 16 out of 100 individuals without. [No standardization for parents' age was attempted.]

Additional information was obtained from the incidence of hypertension in grandparents. Among mothers with both parents hypertensive the incidence of hypertension was 22%, with one parent hypertensive 10%, and with normotensive parents 4%. Among fathers the difference in incidence of hypertension between the three groups was less conspicuous. There was a higher incidence of hypertension in mothers and of coronary disease in fathers of hypertensive subjects. The familial pattern did not support the theory that hypertension is transmitted through a single dominant gene [unless very limited penetrance is postulated], and the author concludes that while the findings are consistent with transmission through a widely-distributed recessive gene, a more complex genetic mechanism is probably involved.

R. H. Cawley

Industrial Medicine

1149. **Occupational Leukoderma. With Report of Cases**
J. V. KLAUDER and J. M. KIMMICH. *Industrial Medicine and Surgery* [*Industr. Med. Surg.*] **22**, 106–110, March, 1953. 6 figs., 13 refs.

Occupational leucoderma consists of patches of depigmentation of skin due usually to contact with rubber articles such as gloves and aprons. The cause of the depigmentation is "agerite alba", a trade name for monobenzyl ether of hydroquinone. This antioxidant is incorporated as preservative in many rubber articles. It is soluble in water at an alkaline *p*H, and thus sweat increases its effect. The depigmentation is most noticeable in negroes. In some cases it has been associated with a mild inflammatory reaction; personal susceptibility also plays a part. The dopa reaction is negative in the depigmented areas, but becomes positive after repigmentation. General health usually remains unaffected. Pigmentation begins to return soon after the offending article has been discarded. Loss of hair over the affected areas has been reported in a few cases.

The authors, after reviewing the literature, present 8 cases occurring in negroes out of a total of 20 working under identical conditions and using the same yellow "neoprene" aprons. White spots began to appear on skin areas in contact with these aprons after about a month's exposure, and then coalesced to form patches of diffuse leucoderma. No dermatitis was present. After the issue of a new set of aprons specified not to contain any agerite alba, pigmentation began to reappear, but 20 months later had not yet completely returned.

In discussing the differential diagnosis the authors state that the depigmentation due to monobenzyl ether of hydroquinone is indistinguishable from vitiligo; it also resembles the late dyschromic and vitiliginous lesions of pinta and the terminal stage of pellagrous dermatitis.

Ferdinand Hillman

1150. **The Radiological Appearance of the Lung in Certain Rare Forms of Pneumoconiosis.** (Über die Lungenstruktur im Röntgenbild seltener Pneumokoniosen)
R. HAUBRICH and B. SCHULER. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Rontgenstr.*] **78**, 272–281, March, 1953. 10 figs., 9 refs.

While established silicosis presents a fairly characteristic radiological picture, the earlier stages (especially in the less common forms of pneumoconiosis) may present considerable difficulties in differential diagnosis. In this paper from the University Medical Clinic, Bonn, the authors attempt to analyse the finer lung structure in rare forms of pneumoconiosis as seen in radiographs; they distinguish three types.

In the first, illustrated by carborundum pneumoconiosis (of which they had 8 cases), there is widening of the mediastinal and hilar shadows, with thickening of the normal linear markings similar to that encountered in ordinary bronchitis and bronchiectasis. Later, emphysematous bullae may develop. In one severe case there was a dense reticular pattern with superimposed massive shadows, the appearances being similar to those seen in aluminosis of the lung and pulmonary lymphogranulomatosis.

The second type of picture, as seen in soot pneumoconiosis (6 cases), presents a very fine reticular pattern with minute miliary shadows. The miliary shadows are attributed to deposits of soot at the bronchiolar divisions. Similar appearances are shown in cases of honeycomb lung and of Boeck's sarcoid, and have also been seen in Hodgkin's disease of the lung and lymphangitis carcinomatosa.

In the third type of picture minute opacities predominate, giving a fine stippled appearance. This occurs mainly in ochre pneumoconiosis, in the pneumoconiosis of Siegerland iron-ore miners, and in siderosis of foundry workers. An identical appearance may also be seen in haemosiderosis and in some cases of Boeck's sarcoid.

The authors conclude that although these early radiological patterns are characteristic, differential diagnosis from other conditions cannot be made from the radiograph alone.

[It seems unwise to describe "characteristic" patterns of rare forms of pneumoconiosis on the basis of so few cases. The chief value of this paper lies in the good reproduction of the illustrative radiographs.]

C. M. Fletcher

1151. **Pneumoconiosis from Graphite Dust.** (Pneumokoniose durch Graphitstaub)
H. G. GÜTTNER. *Zentralblatt für allgemeine Pathologie und pathologische Anatomie* [*Zbl. allg. Path. path. Anat.*] **90**, 108–115, April 20, 1953. 2 figs., 27 refs.

1152. **Changes in the Bronchi in Silicosis and Silicotuberculosis.** (Über Bronchialveränderungen bei der Silikose und Siliko-Tuberkulose)
G. WORTH and W. HEINZ. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **78**, 263–272, March, 1953. 9 figs., bibliography.

In this paper the authors describe the results of bronchography performed with water-soluble contrast medium in 50 cases of silicosis, among which were 8 cases of silico-tuberculosis, treated at the Bethamien Hospital, Moers, Lower Rhine. A variety of abnormalities were demonstrated, many of which had not been suspected from plain radiographs and tomograms. These took the form of irregularities of the lumen; bronchiectasis, often with fine atelectasis; bronchial obstruction; cavity formation; gross distortion; and delay in filling

and reabsorption of the medium. These abnormalities were most marked in cases of massive silicosis and silico-tuberculosis.

The authors claim that these observations throw valuable light on the functional state of the bronchial tree in silicosis, and explain the frequent leucocytosis and raised erythrocyte sedimentation rate observed in some patients. The segmental localization of massive fibrosis can also be defined. *C. M. Fletcher*

1153. **A Haematological Study of Hypoxia in Silicosis.** (Étude hématologique de l'hypoxie dans la silicose)
E. BALGAIRIES and C. CLAEYS. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [*Arch. Mat. prof.*] **14**, 12–18, 1953. 27 refs.

The authors set out to discover whether changes in the erythrocyte count, the size distribution of erythrocytes, or the reticulocyte response to exercise might be used as an indication of hypoxaemia in silicosis. They found no relation between the absence or presence of silicosis or its radiological stage and the total number of erythrocytes or the proportion of erythrocytes less than 6 μ in diameter.

Reticulocyte counts in blood from 164 healthy subjects before and at various intervals after standard exercise were first made in order to establish a mean normal resting and post-exercise count. These were then compared with the counts made under similar circumstances in 157 patients with silicosis; no relation between the radiological stage of silicosis and the proportion of cases showing reticulocytosis above the normal mean was found. In 8 cases of cardiac failure and one silicotic patient with dyspnoea at rest the resting reticulocyte count was greatly raised.

Ventilatory efficiency was estimated in 111 subjects by a Tiffeneau test (maximum volume of air expired in one second). Comparison of the results with the reticulocyte response to exercise showed no correlation, nor was any relation found between reticulocyte response and the maximum level of exercise of which the subjects were capable, or with the severity of oxygen debt incurred. The authors conclude that the occurrence of reticulocytosis following exercise is not suitable to be used as a functional test in silicosis. They were unable to determine the reason for the abnormal response to effort shown by certain subjects.

[The title of this paper seems inappropriate, since apparently no measurements of blood oxygen saturation were made.] *C. M. Fletcher*

1154. **Deafness in Shipyard Workers. Critical Evaluation of Findings in Six Hundred Cases and Diagnosis of Occupational Deafness**
A. I. GOLDNER. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **57**, 287–309, March, 1953. 11 figs., 28 refs.

In this paper is described a study of 600 deafened shipyard workers at Flushing, New York. The author, after referring to work published on the effects of excessive noise in military personnel, points out that the " acoustic hazard " of a pneumatic tool on metal is much the same as the chatter of a machine-gun or an automatic rifle. Hazard is increased when work is done inside a metallic chamber, and the smaller the chamber the greater the risk. Of the 600 patients, 403 had an occupational deafness with the typical audiometric curve; in this group were included some who had a low-tone loss without any other cause than noise to explain it, and elderly men in whom the presence of presbycusis was not clinically confirmed. In the remainder, except for a group of 35 " miscellaneous " cases, there was evidence that an occupational cause together with some other factor was responsible.

Patients with uncomplicated occupational deafness usually complained of deafness and tinnitus, though they seldom noticed the deafness until it was severe. Tinnitus was often more troublesome than deafness, but tended to be less noticeable after years of exposure. Occasionally vague otalgia was complained of. The audiometric curve was of the usual cochlear type, with a fall at first in the region of 2,000 cycles per second (c.p.s.), a further fall at 4,000 c.p.s., and sometimes a rise, for higher tones and a progressive shortening of bone conduction. The greatest loss seemed to occur in the first 5 years of employment; after that, progress slowed down until 20 years or more had elapsed, when normal age change also had to be taken into account. The whisper was lost long before the conversational voice range was affected.

It is suggested that early " fatigue reaction " might be used as a screening method for eliminating workers who would be particularly sensitive to occupational noise. From the author's survey it seems that a pre-existing perforation of the membrane (it is stated that welders not uncommonly suffer from perforation by flying splinters) increases the hazard. On the other hand, patients with an established conduction deafness, such as that due to otosclerosis, are not usually so susceptible to loud noise. Nevertheless, such patients are not immune, and severe acoustic trauma may increase their deafness by adding a cochlear element. In some cases head injury, of which there were 27 cases, seems to have accelerated the progress of the deafness, or even to have started it; it is pointed out that there need not be any fracture of the base of the skull in such cases. In one case there was evidence that a sudden " explosive-type " sound increased an already present occupational deafness; in this instance the ear was pressed against a bulkhead when the full impact of a " chipping gun " struck the other side of the bulkhead.

Methods are suggested for diminishing the incidence of this trouble, among them pre-employment examination, elimination of " poor risks ", improved industrial design and sound-proofing, and the provision of efficient ear-protectors. *F. W. Watkyn-Thomas*

1155. **Methyloctylbenzenesulphonate: a New Industrial Sensitizing Agent**
C. N. D. CRUICKSHANK and H. HOWARD-SWAFFIELD. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **10**, 121–124, April, 1953. 2 figs., 6 refs.

Anaesthetics

1156. **The Problem of Anaesthesia for Thoracoplasty**
A. R. HUNTER. *Diseases of the Chest* [*Dis. Chest*] **23**, 197–206, Feb., 1953. 14 refs.

In this paper the controversy about the respective merits of general anaesthesia and local analgesia for thoracoplasty is reopened. The author, who is anaesthetist at the Manchester Royal Infirmary and Baguley Sanatorium, Manchester, began his investigation with a pilot study using several different techniques, from which he decided that the best method was induction with a short-acting barbiturate (thiopentone, thialbarbitone) and maintenance with nitrous oxide and oxygen, with curare for relaxation, employing an endotracheal tube and, when required, postoperative bronchoscopy. On the basis of this finding general anaesthesia was induced 259 times in 126 patients undergoing thoracoplasty: 99 upper-stage, 72 second-stage, 32 third-stage, and 45 anterior-stage operations; other operations (mostly revision operations or laying open an empyema cavity) numbered 11. One patient, operated upon before the advent of streptomycin, died of tuberculous bronchopneumonia; no other deaths occurred within 2 months of operation. It is known to be difficult to assess the spread of the tuberculous process and to attribute its occurrence to any one technique. In the present series serious spread occurred in only 1·5% of cases, while after 4·6% of operations (that is, 9·5% of patients) there was extension of disease as seen radiologically within 2 months of operation—4 cases of bronchopneumonia, 7 of reactivation or extension in the contralateral lung, and 1 of reactivation in the same lung.

[The figures given above compare favourably with other figures quoted in this paper, and bear out the general impression that in skilled hands modern methods of general anaesthesia are as safe as local analgesia in thoracoplasty. The author fails to stress the considerable reduction of haemorrhage gained with local analgesia, although he refers to adequate replacement by transfusion.] *D. D. C. Howat*

1157. **The Anti-curare Agents**
A. R. HUNTER. *British Medical Journal* [*Brit. med. J.*] 1, 640–642, March 21, 1953. 8 figs., 11 refs.

The only safe remedy for respiratory depression due to curarizing drugs is artificial respiration. This, however, may be inconvenient. Neostigmine is an adequate and effective drug, but several fatalities have resulted from its use. "Tensilon" (3-hydroxyphenyl-dimethylethyl ammonium iodide) has been used in the United States as an anti-curare agent. It is free from the excessive parasympathetic stimulation of neostigmine, but its action is transient and relapse may occur within 10 minutes. Neither antidote is completely satisfactory, but as neostigmine is the more effective it was investigated to elucidate its dangers.

A series of 50 curarized patients at the Royal Infirmary, Manchester, were given neostigmine, and their pulse rate was counted repeatedly to obtain information on the following points: (1) the effect of neostigmine with atropine; (2) the effect of neostigmine with atropine given previously; (3) the effect of the same mixture with a sympathomimetic drug; and (4) the amount of atropine required to make the neostigmine safe.

In every case given neostigmine and atropine together the pulse rate accelerated, bradycardia sometimes developing later. When atropine had been given some time before the neostigmine the rate accelerated and then slowed as before. The addition of a vasopressor to the antidote mixture produced a greater acceleration, but the later slowing remained unaltered. The danger point in the administration of neostigmine was found to be difficult to define. A pulse of 50 may be physiological or it may indicate a profound vagal effect. It was assumed, however, that a pulse of 50 after the administration of neostigmine represented a dangerous degree of bradycardia. No patient who had 1/50 gr. (1·3 mg.) of atropine developed this degree of bradycardia even with doses of 2·5 mg. of neostigmine. Atropine caused slowing of the pulse rate when given hypodermically, but not when given intravenously.

The author concludes that bradycardia following the administration of neostigmine alone may be treated by giving quickly at least 1/100 gr. (0·65 mg.) atropine intravenously. He recommends that no patient to whom neostigmine has been given should be left unwatched for at least 10 minutes. *W. Stanley Sykes*

1158. **A New Antagonist to Syncurine**
L. D. VANDAM, P. SAFAR, and P. R. DUMKE. *Current Researches in Anesthesia and Analgesia* [*Curr. Res. Anesth.*] **32**, 113–122, March–April, 1953. 5 figs., 11 refs.

"Compound 49–204" (1-methyl-2-(4′-dimethylaminophenethyl)-piperidine-1 : 4′-bis-methiodide), which is an analogue of "syncurine" (decamethonium; "C10"), was tried upon conscious and anaesthetized subjects as an antagonist of C10. [The structural formula of this is given correctly in the text, but in the legend the piperidine ring is erroneously described as a stilbazoline ring.]

In 35 anaesthetized patients apnoea was deliberately produced by thiopentone and C10. Intravenous injection of 100 mg. of Compound 49–204 produced a striking response in 17 patients: diaphragmatic contractions were restored to normal in 3 to 4 minutes, and coughing and movements demonstrated the central stimulation produced by the drug. In the other 18 patients no definite effect was observed, although an additional dose of 50 mg. produced respiratory stimulation in some of them, suggesting that the original dose had been insufficient. The effect of Compound 49–204 was most marked in

patients who had received only small doses of thiopentone. In a further 10 patients anaesthetized with ether and having respiratory depression produced by C10, injection of 50 to 150 mg. of Compound 49–204 restored the respiratory volume to normal within a minute or two without affecting the respiratory rate. The antagonist was more effective in the presence of ether than of thiopentone, which is a central depressant. After the initial reversal of the effect of C10, further doses of Compound 49–204 decreased respiratory exchange, suggesting that the drug had a curare-like action of its own.

In 5 conscious subjects vital capacity and hand-grip strength were measured at 10-minute intervals and doses of C10 and Compound 49–204 injected intravenously. The antagonist produced rapid reversal of the effects of C10 at all stages in the course of its action. A dose of Compound 49–204 had a protective action which lasted for 30 minutes against subsequent injections of C10. The antagonist, when given alone in doses of 100 to 350 mg., produced difficulty in focusing the eyes, ptosis, a sensation of intense bodily warmth, and sometimes dryness of the mouth, sweating, and weakness. There was also a slight, transient diminution in hand-grip strength with a moderate degree of sinus tachycardia, but no change in respiration or blood pressure. A dose of 100 mg. of the drug did not augment the muscular paralysis produced by 9 mg. of D-tubocurarine.

The authors consider that Compound 49–204 may be useful in counteracting respiratory depression resulting from neuromuscular blockage and may also be of value in other types of apnoea because of its central stimulatory effect. Large doses of the drug might be expected to have an adverse curare-like action during ether anaesthesia or following administration of D-tubocurarine, or in myasthenia gravis, but the difference between the dose producing reversal of action of C10 and the dose producing curare-like effects seemed to be wide. *L. G. Goodwin*

1159. **Control of Postoperative Pain**

A. H. IASON and H. E. SHAFTEL. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] **19**, 215–224, Feb., 1953. 4 figs., 19 refs.

The authors, writing from Brooklyn, New York, describe a number of techniques using "efocaine" to reduce postoperative pain. Efocaine consists of procaine base and butylaminobenzoate dissolved in propyleneglycol. On contact with tissue fluids the solutes are precipitated as a microcrystalline deposit, which is gradually absorbed while exercising an analgesic effect for about 10 to 14 days. The organic solvent is rapidly dispersed. No tissue damage from its use has been demonstrated.

Injections are made while the patient is still in a stage of general anaesthesia, as they are painful. Most extradural nerve blocking or infiltration routes are available and are well known, the former being considered the more effective. Very accurate placing of the needle is essential, as there is no diffusion of the deposit. Injections of 1 to 3 ml. are made at a point on each nerve. [The danger of pneumothorax from pricking the lung during intercostal injection is not adequately indicated.] The authors advise that during infiltration "pooling" is to be avoided: a thin line of solution should be deposited. Frequent aspirations should be made, and if a vessel is entered, firm pressure should be applied to avoid a haematoma. Intradermal deposits and infiltration of the deep tissues should also be avoided. It is recommended that efocaine injections should not follow extensive infiltration with aqueous local analgesic solutions. In the authors' series of 584 cases 43·3% needed no postoperative medication, 39·5% had 1 or 2 doses, 12·5% had 3 or 4 doses, and 5% over 4 doses. The average number of doses per patient was 1·64 as compared with 4·83 in a control group. *E. K. Brownrigg*

1160. **Oenethyl in Spinal Anesthesia**

N. ZELDIS. *Current Researches in Anesthesia and Analgesia* [*Curr. Res. Anesth.*] **32**, 27–36, Jan.–Feb., 1953. 11 refs.

The efficacy of 2-methylaminoheptane ("oenethyl") in counteracting the hypotension produced by spinal analgesia has been compared with that of ephedrine and of phenylephrine ("neosynephrine"). The first of these drugs was given to 150 patients and the other two, separately or together, to 184 patients at Mount Sinai Hospital, Hartford, Conn. The criterion of effectiveness was the number of additional doses of the vasopressor agent needed to maintain blood pressure at a safe level. One or more additional doses of 2-methylaminoheptane were necessary in only 3 cases, whereas with ephedrine additional doses were required in 17 cases.

Such variables as height of analgesia, duration of operation, and amount of haemorrhage make strict comparison difficult, but an attempt is made to overcome this by presenting the results in a number of different tables. Study of the findings indicated that 2-methylaminoheptane was superior to either of the other two drugs. *Ronald Woolmer*

1161. **Rectal Use of "Pentothal" as Basal Hypnotic in Pediatric Surgery**

W. MIGDAL, A. C. GOLDFEDER, and A. H. KORNBLAU. *Current Researches in Anesthesia and Analgesia* [*Curr. Res. Anesth.*] **32**, 61–65, Jan.–Feb., 1953. 7 refs.

A report is presented on 200 consecutive cases in which thiopentone was administered rectally to children as a preoperative hypnotic at Beth-El Hospital, Brooklyn. The drug was given in 10% solution in normal saline or 5% glucose in saline, the dosage being 1 g. per 75 lb. (35 kg.) body weight, with a maximum dose of 1 g.; atropine was also given as a routine. Induction was followed by one or other of the usual anaesthetic procedures, except in 2 cases in which local infiltration with procaine was carried out.

Of the results in the 200 cases, involving a variety of surgical procedures, only 5 were classified as "poor" in that the child cried, struggled, or remained awake; but even in these there was subsequent complete amnesia for the visit to the operating theatre. Because smaller amounts of the agents subsequently used were needed, recovery was rapid and there was less postoperative nausea and vomiting. *Donald V. Bateman*

Radiology

1162. **Hematologic Studies of Irradiated Survivors in Hiroshima, Japan**
Y. YAMASOWA. *Archives of Internal Medicine* [*Arch. intern. Med.*] **91**, 310–314, March, 1953. 5 refs.

This report is a hematologic survey conducted 33 to 44 months after the detonation of the atomic bomb in Hiroshima, Japan. The hematologic findings on a total of 824 survivors are compared with those on a control group of 1,145 residents of Kure. Although statistical differences are apparent in the two groups, when one takes into account errors inherent in the hematologic methods themselves and differences in the possible incidence of parasitism and nutrition, it would be unwarranted to attribute the slight changes found to radiation effect.

The data presented here seem to indicate that radiation resulting from the explosion of the atomic bomb in Hiroshima, on Aug. 6, 1945, has not significantly varied the hematologic values as analyzed in this report over a three- to four-year period.—[Author's summary.]

RADIODIAGNOSIS

1163. **Clinical Experience with the Water-soluble Bronchography Compounds**
M. E. PECK, A. J. NEERKEN, and E. SALZMAN. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **25**, 234–245, March, 1953. 4 figs., 24 refs.

One of the water-soluble contrast agents was used for bronchography in 56 cases at the University of Colorado Medical Center, and in the present paper the authors review their findings. Of these 56 bronchograms, 19 (34%) were considered to be unsatisfactory, compared with 83 out of 528 (16%) taken with iodized oil (" lipiodol "). The authors offer several explanations for this variation, including the different technique and different interpretation applied with the newer agents and the fact that bronchospasm is more likely to arise, especially if local analgesia is not employed,

Two fatal cases in which water-soluble media were used are described. Death was due to anaphylactic shock, and the suspending agent for the diodone (methylcellulose) was thought to be responsible in each case.

[In Britain in 1952 Don described his experiences with a water-soluble agent (*Brit. J. Radiol.*, **25**, 573); he found the cricothyroid route the most satisfactory. The abstracter's own limited experience has not convinced him that the advantage of obtaining clearing of the lung is greater than the disadvantages encountered.]

Sydney J. Hinds

1164. **Kymography of Diaphragm**
M. E. GALARZA. *Diseases of the Chest* [*Dis. Chest*] **23**, 313–319, March, 1953. 24 figs., 7 refs.

1165. **Errors and Pitfalls in the Radiological Diagnosis of Intestinal Obstruction due to Stenosis of the Colon.** (Erreurs et pièges du radiodiagnostic appliqué aux occlusions intestinales par sténose colique)
C. OLIVIER and N. ARVAY. *Presse médicale* [*Presse méd.*] **61**, 259–262, Feb. 25, 1953. 12 figs.

The diagnosis of colonic obstruction by means of plain radiographs is generally thought to be easy, but as the authors point out, mistakes are inevitable unless examination by barium enema is performed in every case. In the common left-sided obstruction both large and small intestines usually show gas and fluid levels, the caecum in most cases being the most distended segment. Occasionally only the large intestine is distended, probably because the ileo-caecal valve remains competent and resists back-pressure. Caution is here essential because it is just in this type of case that a perforated caecal ulcer may occur. Very rarely, although it is the left side of the colon which is obstructed, distension is limited to the small intestine. No theoretical explanation for this is suggested.

Radiologists are reminded that a barium enema sometimes flows readily upwards above a stricture; and that unless radiographs are taken before this happens, it may be impossible to make a definite diagnosis.

Denys Jennings

1166. **The Differential Diagnosis of Ileus of the Small Intestine.** (Zur Differential-diagnose des Dünndarm-Ileus)
E. FREEB. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Rontgenstr.*] **78**, 141–152, Feb., 1953. 9 figs., 22 refs.

In this paper from the Radiological Department of the Marien Hospital, Stuttgart, the author expresses the opinion that all patients being examined for ileus of the small intestine should be screened, and that fluid levels can be shown only with a horizontal beam. If the patient is unable to stand, he can be screened lying on his side. The movements of the diaphragm should be checked, and the absence of gall-stones confirmed by radiography. In these cases three questions have to be answered: (1) Is there an obstruction? (2) Where is it situated? and (3) What is the likely cause?

The presence of air in the small intestine is abnormal. In a pyknic subject with a horizontal stomach swallowed air may reach the upper small intestine, but the bubbles are small and the condition is easily recognized. In cases of colonic dysfunction, or after enemata, or even after large doses of saline aperients, there may be fluid levels in the colon and sometimes small amounts of gas pass into the lower ileum. In steatorrhoea and in acute enteritis collections of gas and the presence of fluid levels in the small intestine are common, but if the patient is screened the picture is seen to be a changing one: part

of the small intestine in contact with an inflamed viscus often contains air, and acute pancreatic necrosis [also a splenic infarct] may lead to considerable distension of loops of jejunum in the upper left quadrant. In paralytic ileus there is a tendency for the whole gut to be distended.

The most important sign of mechanical obstruction is the way in which the gut below the obstruction empties itself. Normally the colon always contains gas; when there is obstruction in the lower ileum the central " ladder " pattern contrasts with the absence of colonic shadows in the periphery. The valvulae conniventes are the main aid in location, being most marked in the mid-jejunum, but with gross distension they are of course obliterated.

[In the abstracter's experience the classic *x*-ray appearances of obstruction are usually masked if the patient has been given an enema before he is sent to the radiological department. Radiology is a valuable method of investigating the cause of pain, but it is no use waiting until the next day or until various treatments have been tried.] *Denys Jennings*

See also Respiratory System, Abstract 1056; and Industrial Medicine, Abstracts 1150 and 1152.

RADIOTHERAPY

1167. **A Critical Review of the Treatment of Haemangioma.** (Kritische Betrachtung zur Praxis der Hämangiombehandlung)
E. H. GRAUL. *Strahlentherapie* [*Strahlentherapie*] **89**, 409–432, 1952. 26 figs., 39 refs.

On the basis of 4½ years' experience at Münster University Skin Clinic, during which time about 900 new cases of haemangioma a year were treated, the author is led to reject the following techniques since they lead to recurrences or poor cosmetic results: treatment by surface or interstitial radium, injection of sclerosants or boiling water, carbon dioxide snow, surgical ligation or excision. In his view " spider " angioma is best treated by electrocoagulation of the central vessel. Cavernous angioma is best treated by short-distance *x*-ray therapy with the Chaoul type of apparatus, the high dose rate being of great advantage in the treatment of infants. Very thick tumours need higher kilovoltage. Most workers give from 500 to 600 r, but this causes ulceration in one-third or one-fourth of cases. At Münster an initial dose of 150 r is now used, to test sensitivity; a month later, if there has been little or no change, 350 r is given; if there is a definite response the dose of 150 r is repeated. Another dose of 350 r is given after a further month, these 3 doses usually being enough, although older subjects may need 4 or 5; the total dose is 800 to 1,500 r. After an interval of 9 months a second course may be needed for the larger lesions, when single doses of 350 r are used.

The optimum age to begin treatment is 6 to 8 weeks. If the lesion is mixed capillary and cavernous, the cavernous part should be treated first. Capillary angioma (port-wine stain) is best treated by Grenz rays (10 to 12 kV), but the results are not generally so good as in cavernous angioma; 1,000 to 1,500 r is given every 2 weeks to a total dose of 9,000 to 10,000 r, and the course may be repeated annually. Thorium-X has not proved so useful, as its penetration is too low. Lesions of the Sturge–Weber syndrome are unusually radiosensitive. Hyperkeratotic elements of angiomata are resistant, and respond only to high dosage (4,000 to 5,000 r). *J. Walter*

1168. **Radiotherapy of Tumours of the Skin, 1935–49.** (Die Röntgenbestrahlung der Hautgeschwülste in den Jahren 1935–1949)
W. GREVE. *Strahlentherapie* [*Strahlentherapie*] **89**, 401–408, 1952. 6 figs., 3 refs.

A total of 644 cases of primary cancer of the skin were treated by short-distance *x*-ray therapy at Berlin University Röntgenological Clinic between 1935 and 1949. The types of apparatus used included those of van der Plaat and of Chaoul. The author deprecates the use of single-dose treatment, which should be confined to emergency cases. The usual dose was 600 to 700 r at each treatment, to a total of at least 6,000 r, or in the case of precancerous lesions up to 2,000 to 3,000 r. Postoperative treatments require similar dosage.

At least 91% of patients remained symptom-free, the cure rate in 46 cases of cancer of the lip being 100%. Of 22 patients with malignant melanoma, 21 remained symptom-free, as compared with a death rate of 64% after postoperative irradiation; in these cases dosage must be high—10,000 to 12,000 r. Irradiation is of little value for benign melanoma with an occasional degree of paling and epilation. It is, however, of great value for haemangioma; in such cases 3 or 4 doses of 300 to 400 r were given at intervals of several days. Of 190 cases followed up, 158 had excellent cosmetic results, 19 moderate pallor, and 13 patchy depigmentation. At this clinic treatment by short-distance *x*-irradiation has practically displaced therapy by surface radium.
J. Walter

1169. **The Treatment of Cerebral Gliomas with 24-million-volt *X* Rays**
D. A. LAYNE, V. LOGUE, W. V. MAYNEORD, W. MCKISSOCK, and D. W. SMITHERS. *Lancet* [*Lancet*] **1**, 516–519, March 14, 1953. 5 figs., 13 refs.

In 1949 a 20- to 30-million-volt electron-synchrotron was installed at the Royal Cancer Hospital, London, and in the present paper the first clinical application is described. Physical studies showed the maximum dose to be achieved not at the surface, as with conventional deep *x*-ray therapy at 200,000 volts, but at a depth of 3·5 cm. with 24-million-volt energy. The surface dose was about 30% of the maximum—a considerable clinical advantage. Another advantage was the relatively low absorption in bone as compared with deep *x*-ray therapy. Total energy absorption by the patient was also less, and tests showed that very small amounts of radiation were received by the staff (about 0·02 r per week). Collimation of the beam proved troublesome and a new, elaborate, and expensive system was finally adopted. It is pointed

out that at these high energies atomic nuclear interactions can occur and be of possible biological significance; measurements showed, however, that not more than 1% of the energy absorbed was due to such effects. In preliminary biological experiments at the Strangeways Laboratory, Cambridge, no important differences in biological efficacy were found as compared with conventional radiations. The advantages of these radiations rest, therefore, on the superior physical distribution of absorbed energy in the tissues.

Treatment was started in May, 1950, with an output of 5 r per minute at 1 metre. Ten cases of cerebral glioma were chosen, because of the presence of bone, the poor prognosis in such cases, and the relative accuracy of location, and progress is reported up to December, 1952. The dose aimed at was 7,000 r in 7 weeks by an accurately directed small-field technique. No general reaction or radiation sickness was seen, and variations in blood count were negligible. Local reactions were much less than with similar doses given at lower voltages. Epilation occurred at 1,800 to 2,000 r, with occasional faint erythema. Hair always grew again within 4 months. Of the 10 patients, 9 are alive, many well and working; immediate palliation was not only good, but superior to that achieved with any other technique previously used. *J. Walter*

1170. **Carcinoma of the Eyelids**
B. ROSEBERG. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **69**, 196–207, Feb., 1953. 37 refs.

After briefly discussing the incidence, aetiology, pathology, and clinical aspects of carcinoma of the eyelids, as well as various treatment techniques and radiation-induced complications, the author reviews the results of treatment of 102 lesions of the eyelids out of 133 lesions in 131 patients seen at the State University Hospitals, Iowa City, from 1930 to 1943 inclusive, 31 lesions being excluded because of loss of contact with, or death of, the patient. Four general methods of irradiation were used: radium plaque, deep *x*-ray therapy at 200 kV, intermediate therapy at 100 to 135 kV, and short-distance low-voltage therapy at 60 kV. The great majority of cases were treated at medium and low voltages. The usual doses given at 100 kV varied from between 1,000 and 2,000 r in a single dose up to 5,000 r in divided doses. The single dose at 60 kV varied from 1,500 to 3,000 r according to size of lesion; the larger lesions were treated with a daily dose of 500 r or even 1,000 r up to a total dose of 6,000 to 7,000 r in 14 days.

The results of treatment are discussed in two groups. Group 1 (" healed ") includes all cases having no residual or recurrent neoplasm for 3 or more years after the last treatment, and Group 2 (" not healed ") includes all other cases. Of 41 lesions treated by intermediate therapy 36 were " healed "; and of 39 lesions treated at 60 kV the number remaining " healed " was again 36. Of 8 lesions treated with a radium plaque, only 3 were controlled. Lesions situated at the lateral canthus responded best, while lesions of the upper and lower lids responded less well. In the case of 36 lesions additional treatment was required. These lesions seemed to respond better if previously treated by intermediate or deep therapy; those previously treated by low-voltage therapy responded less well, and lesions formerly treated by radium responded poorly, to additional treatment.

[A comprehensive review of this kind remains incomplete without a definite statement as to the incidence, if any, of radiation-induced scarring and deformities around the eyelids or possible ocular damage.]
Jan G. de Winter

1171. **Transvaginal Cone Roentgen Irradiation in Cancer of the Cervix Uteri. Report of Twelve Years' Experience**
J. Y. HOWSON, B. P. WIDMANN, and J. L. WEATHERWAX. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **69**, 182–190, Feb., 1953. 11 refs.

In this paper are reported 225 cases of cervical cancer treated at the Philadelphia General Hospital between 1938 and 1950 by means of intravaginal high-voltage *x*-irradiation as a supplement to the usual external radiotherapy. These cases were distributed according to stage as follows: Stage I, 6; Stage II, 33; Stage III, 111; and Stage IV, 61; there were also 14 cases of stump cancer. The majority received external therapy first. This was given in a dose of 200 kV on alternate days with 150 r (in air) to each of 4 fields measuring 15 by 20 cm. up to a total tumour dose of 2,000 r (in air). On completion of the external irradiation intravaginal *x*-ray therapy was begun. A dose of 500 r (in air) was given at 200 kV 3 times weekly by means of an intravaginal cone varying from 2·5 to 3·6 cm. in diameter up to a total dose of 8,000 to 12,000 r (in air). A second course of external irradiation similar to that described above was given 6 to 8 weeks after completion of transvaginal therapy.

The results of treatment are quoted in terms of " average duration of life ". Of 111 patients with Stage-III cancer 86 died, the average duration of life being 23·7 months; 25 patients in this group are still alive, representing an average survival of 7 years after treatment. The average duration of life in Stage-II cases was 35·5 months, and in Stage-IV cases 13·6 months.

There were 6 cases of intestinal obstruction attributable to radiotherapy in this series; in addition, the combined incidence of recto-vaginal and vesico-vaginal fistulae was 4%.

The advantages claimed for this combined method of *x*-ray treatment include: (1) first and foremost, increased longevity; (2) marked local improvement, which becomes apparent in most instances by the end of the course of transvaginal treatment; and (3) only a very mild systemic reaction during treatment, consisting at most of a temporary moderate proctitis or a mild cystitis, with absence of nausea and vomiting.

[It is difficult to see how transvaginal *x*-irradiation can be more effective in treating the cervix than radium; in other words, how irradiation by *x* rays of a 3-cm.-thick pencil of tissue along the central axis of the vagina can prove superior to effective irradiation of the whole vaginal vault by gamma rays. It is even more difficult

to accept an avowedly palliative procedure which can produce the calamity of radiation-induced intestinal obstruction in no fewer than 6 cases out of 225. Finally, the unfortunate choice in this report of the "average duration of life" (by itself almost meaningless) as sole index of therapeutic success in the great majority of cases precludes proper critical evaluation of the palliative technique described; for this index fails to give any definite indication as to the measure of useful palliation (for example, the period of *symptom-free* survival) obtained in the individual case by a method which, for all that we are told, may merely prolong the act of dying.]

Jan G. de Winter

1172. **Ewing's Sarcoma. A Study of Fifty Cases Treated at the Massachusetts General Hospital, 1930–1952 Inclusive**

C. C. WANG and M. D. SCHULZ. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 571–576, April 2, 1953. 10 refs.

The results of treatment in 50 cases of Ewing's sarcoma seen at the Massachusetts General Hospital between 1930 and 1952 are analysed. Of the 50 patients, 7 lived for 5 years or more, 6 of them after radiotherapy and one after surgery; only 5 of the 7 were apparently cured.

Supervoltage *x*-ray therapy was given in the majority of cases, the dose being 200 to 300 r (in air) per day to a total tumour dose of between 3,000 and 6,000 r. The area treated included, as a rule, the entire bone where the growth was situated, regardless of the apparent size of the tumour.

It is held that *x*-ray therapy achieves results comparable with those of surgery, but without mutilation; for this reason it is superior to surgery in cases of Ewing's sarcoma, especially as this tumour is highly radiosensitive. This palliative treatment is considered worth while in patients with distant metastases; pain and discomfort are relieved and life is often prolonged. It is also suggested that vigorous *x*-ray therapy of solitary metastatic lesions in the lungs is justifiable, the aim in such cases being cure rather than palliation.

Jan G. de Winter

1173. **Prognostic Characteristics of Fibrosarcoma.** (Prognostische Kennzeichen der Fibrosarkome)

M. GOES. *Strahlentherapie* [*Strahlentherapie*] **89**, 373–396, 1952. 42 refs.

The author reviews a series of 79 verified cases of fibrosarcoma of soft tissue of the locomotor system treated at Frankfurt-am-Main Röntgen Institute in the period 1926–50. Brief details of each case, with radiation dosage, are given. Deep *x*-ray therapy was at 180 kV, mostly in divided doses. With the aid of a series of tables the author draws prognostic conclusions based on the clinical findings. Growths not exceeding a hen's egg in size offer the best prognosis, and these may even be curable by radiation alone. The more superficial the position, the better the prognosis.

Best results in treatment were achieved by excision followed by irradiation (3,000 r at the level of the tumour). Small superficial tumours were found to require at least 3,000 r (in air) at the skin surface; tumours as large as a man's fist need 6,000 r; the combination of excision and irradiation secured a 5-year survival in over half of the cases. Other observations and conclusions were as follows. Regression may continue for months or even years; residues should be excised; ulceration is of bad prognostic import. The best treatment of regional-node metastases is excision plus irradiation; if such metastases appear within 4 months of starting treatment, death is likely within 2 years. Distant metastases appearing within 4 months usually cause death within 9 months, but irradiation can prolong life if the metastasis is solitary. Recurrences of the primary tumour, even for a second time, do not necessarily make the prognosis hopeless.

J. Walter

1174. **Hypoplasia of Bone Marrow Associated with Radioactive Colloidal Gold Therapy**

T. W. BOTSFORD, H. B. WHEELER, R. A. NEWTON, and W. E. JAQUES. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 788–791, March 7, 1953. 4 figs., 8 refs.

No cases of serious toxicity from the clinical use of radioactive gold (^{198}Au) have hitherto been reported. At the Peter Bent Brigham Hospital (Harvard University) 4 cases of hypoplasia of the bone marrow associated with the therapeutic administration of this isotope were seen, and these are here described.

The first patient had an inoperable carcinoma of the stomach, the tumour being infiltrated with 85 mc. of ^{198}Au. Post-mortem examination 2 months later revealed marked hypoplasia of the vertebral bone marrow. The second patient underwent amputation of the left great toe and radical dissection of the groin for malignant melanoma. When, some months later, extensive involvement of the lymph nodes of the small-bowel mesentery occurred, the tumour mass was infiltrated with 65·5 mc. of ^{198}Au. The patient died 2 months later. Post-mortem examination revealed local areas of necrosis in the vertebral bone marrow with a relatively greater decrease in myeloid elements than in erythroid elements. In the third patient abdomino-perineal resection was performed for carcinoma of the rectum. Metastases developed with peritoneal effusion. Paracentesis was performed and 100 mc. of ^{198}Au was washed into the peritoneal cavity. At necropsy 4 weeks later marked hypoplasia of the vertebral bone marrow was found. The fourth patient, who underwent radical mastectomy for carcinoma of the breast, developed ascites. Oestrogens were given, followed by injection of 150 mc. of ^{198}Au into the peritoneal cavity. Post-mortem examination 3 days later showed widespread dissemination of the disease and a few areas of necrosis in the vertebral bone marrow.

Altogether the authors treated 23 patients with ^{198}Au, 11 receiving less than 50 mc. and 12 (including the 4 described here) receiving 58 to 153 mc.

D. Waldron Smithers

See also Endocrinology, Abstract 1080, and The Rheumatic Diseases, Abstract 1089.

History of Medicine

1175. **William Thomson and the History of the Contagionist Doctrine in Melbourne**
B. GANDEVIA. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 398–403, March 21, 1953. 4 figs., 7 refs.

William Thomson was born in Glasgow in 1819 or 1820 and educated at the Andersonian School of Medicine and the University of Glasgow. He worked for a time with Perry and Stewart of Glasgow (known for their work in distinguishing between typhus and typhoid fevers), and in 1855, at the age of 35, he settled in Melbourne. Like many a great personality of the nineteenth century he was a gifted scholar with wide culture; he was a pathologist, an epidemiologist, and a Baconian scholar. He was, however, resentful of criticism and arrogant.

The present paper, which includes, as an appendix, a list of Thomson's 39 separately published works, is concerned with his part in the introduction to Australia of the contagionist doctrine and the germ theory of disease. There were many views on the nature of typhoid infection, the two chief ones being the contagionist theory as held by Thomson, and the non-contagionist theory of Murchison, who held that the disease was spread by effluvia from decaying organic matter. From his written work on the cause of typhoid, Thomson's opinions can be summarized thus: typhoid could be spread by a "germ", by ambulant patients, and by contamination; there was no evidence to support the tenet of spontaneous generation; and the disinfection of faeces and fomites was essential.

Koch demonstrated the tubercle bacillus in 1882, six years after Thomson, in 1876, had postulated the existence of a living microorganism as being the cause of tuberculosis. Thomson explained the chemical processes of caseation and showed how erosion of a vessel could bring about spread by the blood. He believed that inhalation of dried contaminated sputum was responsible for the spread of the disease: furthermore that if a living organism was the cause of tuberculosis, then experimental work with germicidal agents should be carried out with vigour. When Koch's discovery was announced Thomson, with much vanity, claimed priority for himself for certain aspects of the work; had he not done so, his name would probably be more familiar to-day than it is.

T. Marmion

1176. **Santiago Ramón y Cajal (1852–1934)**
W. H. MCMENEMEY. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **46**, 173–177, March, 1953. 18 refs.

Cajal was not only a great neuro-anatomist, but also a writer, pathologist, philosopher, and patriot. The school of histology he established revolutionized the methods of approach to the problems of neuro-anatomy and influenced the study of physiology and neuropathology. His father, a non-qualified surgeon, was his first teacher. He was exacting and domineering, and Cajal became wayward and secretive, retaining a shy aloofness throughout his whole life. Worried by his son's uncontrolled imagination, dilettantism, and bellicose tendencies, the father apprenticed him to a barber and then to a shoemaker. By the time he was 14 he showed some promise and the austere parent decided to interest him in osteology. Together they raided a cemetery for bones.

Cajal was to become a surgeon and was sent to Saragossa. At this period he absorbed the writings of the French romanticists and of Jules Verne and under their influence wrote prophetically of the adventures of a microbe sailing on a red corpuscle to watch the epic struggle between leucocytes and parasites. Later this little germ found its way to the brain and discovered the secret of thought and of the voluntary impulse.

Cajal saw military service in Cuba, but malaria and dysentery ruined his health. These were followed by cachexia and jaundice, then by haemoptysis. Fifteen months later his health was restored and he was ready and eager to work for the regeneration of his country —his tool the microscope. He married, and he spent what he called his honeymoon with his Verick microscope in an attic which he had equipped as a laboratory. He bought a simple Ranvier microtome and French periodicals, and in 1880 wrote his first paper, on inflammation in the mesentery, cornea, and cartilage, illustrating it with his own lithographs. During his scientific lifetime he produced 287 other monographs and papers and 15 textbooks, earning for himself the title of the "Hercules of Histology". Success and honour followed; he became a national hero, and was even offered a Ministry with Cabinet rank.

In 1887 Don Luis Simarro, the psychiatrist of Valencia, demonstrated to Cajal the methods of Golgi and Weigert–Pal. A year later Cajal was able to show that an axon could, by means of collateral and terminal branches, make contact with a variety of neurones. Later he deduced that the cell bodies and their processes took part in the chain of conduction. He rejected Gerlach's conception of the anastomotic network of nerve processes, and instead supported the "free-ending" theory. In 1903 he had the inspiration of using hot silver nitrate to stain neurofibrils.

In 1889 he demonstrated his preparations in Berlin. Von Köllicker, who had visited Golgi two years earlier, abandoned the reticular theory and learned Spanish to read Cajal's earlier works. The Spaniard had many friends in Germany, among whom were Krause, Virchow, Weigert, Edinger, and Ehrlich. In 1906 he and the Italian Golgi shared the Nobel Prize, but the latter did not return Cajal's friendliness. Cajal visited both America and England. In 1894 he came to London to deliver the Croonian Lecture and was the guest of

Sherrington, who wrote " Cajal reshaped our knowledge of the cellular architecture of the nervous system. He had . . . pulled down much, but he had built up more ".

The author of this paper offers this conclusion on Cajal's character: " This gifted and serious man possessed, I think, all of what he styled the indispensable attributes of the researcher, namely mental independence, intellectual curiosity, perseverance, devotion to country and a desire for reputation ". *Ruth Hodgkinson*

1177. **The Great Epidemics of Antiquity.** (Les grandes épidémies de l'antiquité)
G. BARRAUD. *Presse médicale* [*Presse méd.*] **61**, 501–502, April 1, 1953.

The author, in describing some of the epidemics of ancient times, concedes that it is generally impossible to-day to identify the diseases causing these outbreaks, which brought death and destruction to entire peoples. He emphasizes that the words *pestis* and *pestilentia* found in old documents were used to describe any disease bringing terror, panic, and death to the populations it invaded.

In the Book of Samuel we have the first description of bubonic plague, with an unmistakable reference to its association with rats. The present author discusses the great plague of Athens (428 B.C.) and mentions that bubonic plague, ergotism, typhus, malaria, and dengue have been variously suggested as the disease concerned. Diodorus Siculus described a severe epidemic disease in Syracuse (396 B.C.) which he attributed to the vengeance of the goddesses, to the heat of the season, and to the proximity of the city to marshy ground. Tacitus referred to a considerable epidemic in Rome during the reign of Nero. But better known was the plague of Antoninus, which scourged the entire Roman world and continued with short intervals of abatement for 22 years; it was this epidemic which drove the celebrated Galen from Rome. During the 3rd century A.D. an even more terrible epidemic raged throughout the Roman Empire and lasted about 15 years. St. Cyprian left a description of this disease, the earliest symptoms of which were sore throat and gastro-intestinal upset, but gangrene of the limbs and loss of vision and hearing were common complications. A severe epidemic of a disease resembling anthrax spread over the same empire in A.D. 302. At the beginning of the 4th century A.D. epidemics occurred again and affected not only Italy, but also Gaul, Spain, and even Britain.

The great plague of Justinian apparently originated in Egypt, and appeared in Constantinople in A.D. 543. This disease was associated with buboes and eruptions, and caused an appalling mortality, being said to have carried off as many as 10,000 persons in one day. It appeared in Gaul in 549, probably having gained entrance to that country at Marseilles. Gregory of Tours described it as the " inguinal disease ". So suddenly and mortally did the disease strike in Narbonne in 567 that it was impossible to tell the number who perished. In 582 Gregory described another disease, *la maladie valétudinaire*, now known to have been smallpox, which appeared in Touraine. This malady was associated with violent fever and a vesiculo-pustular eruption. Contemporary documents give indications of the spread of this disease among the Arabs, though it was not until some three centuries later that Rhazes clearly described smallpox.

In the 12th century A.D., largely through travellers returning from the Crusades, the rat was introduced into Western Europe from Arabia and Egypt and, establishing itself securely, brought in its train the great epidemics of bubonic plague which affected European civilization right up to the 17th century. *H. P. Tait*

1178. **Sir Frederick Treves, Bart. (1853–1913)**
W. R. BETT. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **12**, 189–193, March, 1953. 2 figs.

1179. **In Search of Samuel Jackson**
P. CHILDS. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **12**, 173–178, March, 1953.

1180. **The Hunterian Era: Its Influence on the Art and Science of Surgery**
L. E. C. NORBURY. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **12**, 303–327, May, 1953. 12 figs., 24 refs.

1181. **The Impact of Röntgen's Discovery upon the Treatment of Fractures**
L. F. PELTIER. *Surgery* [*Surgery*] **33**, 579–586, April, 1953. 27 refs.

1182. **Early Dundee Doctors**
J. KINNEAR. *Edinburgh Medical Journal* [*Edinb. med. J.*] **60**, 169–183, April, 1953.

1183. **Medical Students through the Ages**
ZACHARY COPE. *St. Mary's Hospital Gazette* [*St Mary's Hosp. Gaz.*] **59**, 96–105, June, 1953. 21 refs.

1184. **" Touching a Cure of an Inveterate Phrensy by the Transfusion of Blood "**
R. J. WEDGWOOD and G. R. RIESE. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 902–904, May 21, 1953. 9 refs.

1185. **A History of Infant Feeding. Primitive Peoples: Ancient Works: Renaissance Writers**
I. G. WICKES. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **28**, 151–158, April, 1953. 4 figs.

1186. **Magic, Medicine, and Religion. The Persistence of an Idea**
S. SMITH. *British Medical Journal* [*Brit. med. J.*] **1**, 847–851, April 18, 1953.

1187. **The Discovery of Western Australia, with Some Early Medical History**
B. C. COHEN. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 840–844, June 13, 1953. 5 refs.

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